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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service • National Institutes of Health • National Cancer Institute

HE 20. 3173/2:

HODGKIN'S DISEASE: DIAGNOSIS AND STAGING

1. LAPAROTOMY IN THE RE-EVALUATION OF PATIENTS WITH ADVANCED HODGKIN'S DISEASE.

Kostraba NC, Peterson BA, Kennedy BJ, Grage TB, Bloomfield CD
(c/o Peterson) Univ. Minnesota Hosp., Box 348, Mayo Memorial Bldg., Minneapolis, MN, 55455
Cancer Treat Rep; 65(7/8):685-687 1981

Twelve patients with advanced nodular sclerosis Hodgkin's disease were extensively reassessed following the completion of planned chemotherapy. The evaluation culminated in an exploratory laparotomy. Eight patients with no evidence of abdominal involvement on noninvasive tests also had no Hodgkin's disease found during laparotomy. Four patients had intra-abdominal Hodgkin's disease suspected prior to laparotomy based on the results of the noninvasive procedures. At laparotomy, benign abnormalities were present in three patients; only one had residual Hodgkin's disease. No patient with a negative laparotomy has developed recurrent abdominal Hodgkin's disease, but two patients developed supradiaphragmatic recurrences. The patient with persistent Hodgkin's disease had his treatment regimen successfully altered. These data suggest that patients with negative preoperative findings do not benefit further from a laparotomy. However, in selected patients with suspicious intra-abdominal findings, the results of laparotomy may alter future management. (Author abstract) (8 Refs)

2. RECURRENT HODGKIN'S DISEASE IN TREATED SITES.

Dolginow D, Colby TV
(c/o Colby) Dept. Pathology, Stanford Univ. Medical Center, Stanford, CA, 94305
Cancer; 48(5):1124-1126 1981

Clinical and pathologic features were assessed in a group of 48 patients with Hodgkin's disease who developed recurrences in treated sites. The histopathologic findings in the initial diagnostic lymph node biopsies were compared with those in the recurrences. Recurrences showed a more pleomorphic appearance and were more difficult to subclassify than the initial diagnostic biopsies. In addition, no histologic features were found in the recurrences that could identify those patients who later died of Hodgkin's disease versus those who were successfully retreated. (Author abstract) (7 Refs)

3. PSEUDOSARCOID GRANULOMAS IN HODGKIN'S DISEASE.

Pak HY, Friedman NB
(c/o Friedman), Cedars-Sinai Medical Center, 8700 Beverly Blvd., Los Angeles, CA, 90048
Hum Pathol; 12(9):832-837 1981

The sarcoid-like granulomas encountered in lymph nodes, spleens, and hepatic biopsy specimens recovered from patients being 'staged' in the course of Hodgkin's disease and, in lower incidence, in non-Hodgkin's lymphomas may, at least in part, be due to reactions to the oily radiographic contrast medium used in lymphangiography. They are seen more often following lymphangiography than when no contrast medium is used. The granulomas in patients who have not undergone lymphangiographic procedures are attributed to the many agents inciting pseudosarcoid lesions. It is speculated that the granulomas seen in Hodgkin's disease after lymphangiography may be the result of a combination of lipogranulomatous reactio n and the effects of an immune adjuvant. (Author abstract) (31 Refs)

HODGKIN'S DISEASE: CLINICAL IMMUNOLOGY AND IMMUNOTHERAPY

4. INCREASED SENSITIVITY OF LYMPHOCYTES FROM PATIENTS WITH HODGKIN'S DISEASE TO CONCANAVALIN A-INDUCED SUPPRESSOR CELLS.

Vanhaelen CP, Fisher RI
(c/o Fisher) Medicine Branch, NCI, NIH, Building 10, Room 12N226, Bethesda, MD, 20205
J Immunol; 127(3):1216-1220 1981

We have studied both the capacity of lymphocytes from patients with active Hodgkin's disease to generate suppressor cells when they are stimulated with concanavalin A (Con A) and the sensitivity of these lymphocytes to the suppression exerted by normal lymphocytes that had been induced with Con A. Lymphocytes were incubated in the presence or absence of Con A, 50 ug/ml, for 48 hr and treated with mitomycin C. Their regulatory activity on the proliferation of fresh allogeneic lymphocytes stimulated by a suboptimal (10 ug/ml) dose of Con A was assayed in a second culture. We found no significant difference between the suppressive activity induced by Con A in lymphocytes from normal individuals (40.1 +-3.2%) and 13 patients with active Hodgkin's disease (35.0 +-3.2%; p greater than 0.12). The proliferative response of the lymphocytes from 20 patients with active, untreated Hodgkin's disease was much more sensitive to the inhibition exerted by normal, allogenic, Con A induced suppressor cells (59.4 +-3.2%) than that of lymphocytes of 30 normal controls (39.8 +-2.4%; p less than 0.001). The sensitivity to suppression was greater in patients with advanced stage of disease (70.4 +-4.8%) than that observed in both normal controls (p less than 0.001) and patients with early stages (53.5 +-3.2%; p = 0.01); the patients with early stages were still significantly more sensitive to suppression than the normal controls (p less than 0.01). The difference in sensitivity to suppression was not caused by the lower proliferation of patients' lymphocytes in response to Con A, since identical results were obtained when normals with low Con A-induced proliferation were selected for comparison. Indomethacin in the second culture did not reverse the suppression, nor did depletion of adherent cells from the responders' lymphocytes. Suppression required the presence of living suppressor cells early in the second culture. Active suppressor cells did not remove Con A from the second culture, nor did they kill the responding lymphocytes. Thus, although lymphocytes of patients with active Hodgkin's disease develop normal suppressor cell activity in response to Con A, they have excessive sensitivity to suppression by Con A-induced regulatory cells. Increased sensitivity to T cell regulation may explain some of the T cell deficits observed in patients with Hodgkin's disease. (Author abstract) (33 Refs)

5. LYMPHOID SUBPOPULATIONS OF PERIPHERAL BLOOD AND SPLEEN IN UNTREATED HODGKIN'S DISEASE.

Posner MR, Reinherz EL, Breard J, Nadler LM, Rosenthal DS, Schlossman SF
Sidney Farber Cancer Inst., 44 Binney St., Boston, MA, 02115
Cancer; 48(5):1170-1176 1981

A panel of monoclonal antibodies with well-defined specificities were used as probes to investigate the phenotypes and lineage of circulating lymphoid cells and splenocytes in untreated patients with Hodgkin's disease. A significant relative and absolute reduction in T cells (anti-T3+) was found only in patients with B-symptoms. There was no alteration in the fraction of helper (anti-T4+) or cytotoxic/suppressor (anti-T5+) T cells circulating in peripheral blood when compared to normals, nor was there activation of these cells as measured by the development of surface Ia (anti-I1+). Circulating T cell subsets were not altered 5 to 14 days after splenectomy. Splenic T cells were increased equally in involved and uninvolved spleen when compared with control spleens obtained from accident victims. These findings indicate that abnormal T cell function in Hodgkin's disease may be the result of subtle alterations in T cells or non-T immunoregulatory mechanisms. (Author abstract) (49 Refs)

6. MULTIVARIATE ANALYSIS OF T-CELL FUNCTIONAL DEFECTS AND CIRCULATING SERUM FACTORS IN HODGKIN'S DISEASE.

Schulof RS, Bockman RS, Garofalo JA, Cirrincione C, Cunningham-Rundles S, Fernandes G, Day NK, Pinsky CM, Incefy GS, Thaler HT, Good RA, Gupta S
Dept. Medicine, Div. Hematology and Oncology, George Washington Univ. Sch. Medicine, 2150 Pennsylvania Ave., N.W., Washington, DC, 20037
Cancer; 48(4):964-973 1981

A comprehensive immunologic and serologic analysis was performed on 31 untreated patients with Hodgkin's disease. Immune evaluations stressed T-cell functional activity and included traditional parameters (PHA responsiveness and delayed hypersensitivity skin reactivity), as well as newer functional assays [T-cell colony formation, chemotaxis, spontaneous and antibody-dependent cytotoxicity, and concanavalin A-induced suppressor cell activity (CISA)]. Serum factors included ferritin, prostaglandins, zinc, copper, immune complexes, and thymic hormone activity. Every patient exhibited at least one T-cell or serum abnormality. The greatest percentage of patients exhibited T-cell defects in chemotaxis (85%), colony formation (81%), and PHA reactivity (64%). Immune defects were more common with advanced disease but were not related to absolute T-cell or monocyte count, skin test anergy, or abnormalities of Tmu/Tgamma cell proportions. Linear relationships were identified among abnormalities in the three assays employing mononuclear cells (PHA, colony formation, CISA) which may have reflected the inhibitory influence of monocytes present in the mononuclear cell preparations. Low serum zinc correlated with marked impairment of T-cell chemotaxis. Elevated prostaglandins were associated with high PHA reactivity and with depressed colony formation. Elevated prostaglandins were associated with high PHA reactivity and with depressed colony formation. Our results indicate that many complex factors, including intrinsic T-cell defects, contribute to the impaired immunity associated with Hodgkin's disease. (Author abstract) (62 Refs)

7. INDICES OF CELLULAR IMMUNITY IN HODGKIN'S DISEASE.

Baisogolov GD, Pavlov VV, Konopliannikov AG, Kozlov VM, Kulish IuS, Iarilin AA, Isaev IG
Res. Inst. Medical Radiology, Obninsk, USSR
Sov Med; (6):29-34 1981

Activity of the peripheral blood T-lymphocytes was studied in 220 patients with Hodgkin's disease. The untreated patients showed progressive decrease of the relative number of T-lymphocytes; the decrease was more pronounced in the patients with advanced disease. The decrease of the absolute number of T-lymphocytes did not depend upon the stage of the disease. 3H-Thymidine incorporation in phytohemagglutinin (PHA)-stimulated lymphocytes showed a stage-dependent decrease. The in vitro indices of immunodeficiency continued to decrease during the radiotherapy and combined treatment. Positive hypersensitivity reaction of delayed type (HRDT) after sc administration of PHA was recorded only in 3.1% of untreated patients (compared with 90% of healthy controls). The intensity of HRDT showed progressive decrease in the patients with advanced disease, compared with the patients with Stage I-II disease. Positive HRDT was recorded in 23.3-25% of the patients undergoing effective treatment and in 40% of the patients in complete remission of 1-42 mo duration. (19 Refs) (In RUS)

HODGKIN'S DISEASE: CHEMOTHERAPY

8. GENERALIZED HODGKIN'S DISEASES: DIAGNOSTIC AND THERAPEUTIC EXPERIENCE.

Branehog I, Ridell B, Rudenstam CM, Weinfeld A, Westin J, Wojciechowicz J
Jubileumskliniken, Sahlgrenska sjukhuset, S-413 45 Goteborg, Sweden
Lakartidningen; 78(26/27):2545-2548 1981

Experience with the diagnosis and treatment of generalized Hodgkin's disease in 31 patients (23 men and 8 women, median age 42 yr) during the period 1970-1977 is reported. Four patients had been pretreated . After clinical examinations and laboratory tests, 5 patients were in Stage I, 11 in II, 8 in III, and 7 in IV. After lymphography, bone marrow biopsy, laparotomy with splenectomy and liver biopsy, the ultimate staging was III in 13 cases and IV in 18. Lymphocyte predominance was found in 2 cases, depletion in 1. All patients received remission induction treatment with six 1-mo courses with the combination of chlormethine, vincristine, procarbazine, and prednisone. The patients who achieved complete remission (CR) received at least three more courses. The patients with progressive disease were switched to the combination of adriamycin, bleomycin, Velbe, and dacarbazine. The patients in Stage IIIA also received radiotherapy. Nineteen patients (2/2 in Stage IIIA, 9/11 in IIIB, 2/2 in IVA, and 6/16 in IVB) achieved CR: 48% of them have remained in continuing CR with a median survival of 58 mo from the start of the treatment. Seven patients have survived at least 5 yr and are considered cured. Eight patients (2/11 in Stage IIIB and 6/16 in IVB) achieved partial remission: six patients died within a short time, but two others remained in partial remission for 22 and 53 mo, respectively. Four patients, all in Stage IVB, did not respond to the treatment: three of them died within 6 mo, another was in relatively good condition for more than 1 yr. (no Refs) (In SWE)

9. ROLE AND PLACE OF POLYCHEMOTHERAPY IN THE TREATMENT OF CHILDREN WITH HODGKIN'S DISEASE.

Makhonova LA, Poliakov VE, Susuleva NA, Il'iashenko VV
Dept. Children's Hematology, All-Union Cancer Res. Center, Moscow, USSR
Pediatriia; (8):36-39 1981

The efficacy of various polychemotherapy regimens was studied in 153 children (95 boys, 58 girls; 2.5-15 yr old) with Hodgkin's disease. The group included 2 patients with Stage I, 74 with Stage II, 56 with Stage III, and 21 with Stage IV. The patients with Stages IIBb, IIIAa, IIIAb, IIIBb, and IV received six cycles of polychemotherapy, compared with three cycles in the patients with Stages IAb and IIAb. The patients with Stages IAa and IIAa did not receive polychemotherapy. Thirty-four children were treated with COPP regimen (cyclophosphamide + vincristine + procarbazine + prednisone), 18 were treated with CVPP regimen (cyclophosphamide + vinblastine + procarbazine + prednisone), and 70 were treated with DOPP regimen (dopane + vincristine + procarbazine + prednisone). Complete remission was recorded in 50% of the children treated with COPP, 55% of the children treated with CVPP, and 67% of the children treated with DOPP. It was recommended that children with Hodgkin's disease should receive reinduction polychemotherapy with 3-mo intervals between the cycles during the first yr after induction, 4-mo interval during the second yr, and 6-mo interval during the third yr. (4 Refs) (In RUS)

HODGKIN'S DISEASE: RADIOTHERAPY

10. MANTLE FIELD IRRADIATION FOR STAGES IA AND IIA HODGKIN'S DISEASE.

Abrahamsen AF, Host H
Norwegian Radium Hosp., Montebello, Oslo 3, Norway
Scand J Haematol; 26(4):306-310 1981

Between 1970 and 1975, 73 patients with surgically staged IA and IIA Hodgkin's disease, localized above the diaphragm, were treated with mantle field irradiation only. Twenty-four patients relapsed during the first 5 yr after the primary treatment, but 14 of them obtained long-lasting complete remission after retreatment. Twenty-three patients with lymphocyte-depleted histology, more than 3 sites involved or a mediastinal mass of more than 6 cm had a high relapse rate (60%); these patients need treatment additional to the mantle field irradiation. The other 50 patients had an 80% relapse-free survival, 96% complete remission after treatment of the first relapse, and 98% survival after 8 yr. We propose that such patients should receive mantle field irradiation only, as the primary treatment. (Author abstract) (25 Refs)

11. MEASUREMENT AND CALCULATION OF OVARY AND FETUS DOSE IN EXTENDED FIELD RADIOTHERAPY FOR 10 MV X RAYS.

Sharma SC, Williamson JF, Khan FM, Lee CK
Dept. Therapeutic Radiology, Univ. Minnesota Hosp., Box 494 Mayo, 420 Delaware St. S.E., Minneapolis, MN, 55455
Int J Radiat Oncol Biol Phys; 7(6):843-846 1981

Ovarian and fetal exposure resulting from extended field radiotherapy (10 millivolt x-rays) for Hodgkin's disease or non-Hodgkin's lymphomas was estimated. Doses received by a phantom loaded with thermoluminescent LiF detectors were measured as a function of distance from the edge of typical mantle, periaortic, and inverted Y fields. Both the periaortic and inverted Y irradiation measurements are applicable to the two oophoropexy techniques used to preserve ovarian function in young women after total nodal radiotherapy: relocation of the ovaries at the midline behind the uterus (1), and lateral transposition of the ovaries to the bilateral iliac wings (2). For periaortic fields, the ovary dose in situation 1 is 0.8%, compared with 0.3% in situation 2. For inverted Y field irradiation, the dose is 3x higher for situation 1. Additional blocking to shield a patient from collimator leakage will reduce the fetal dose significantly for mantle field irradiation. Clarkson's algorithm may be applied with reasonable accuracy to estimate scatter doses for points outside the irradiated vol. (11 Refs)

HODGKIN'S DISEASE: REVIEWS

12. OSTEONECROSIS IN PATIENTS WITH MALIGNANT LYMPHOMA: A REVIEW OF TWENTY-FIVE CASES.

Engel IA, Straus DJ, Lacher M, Lane J, Smith J
Dept. Radiology, Memorial Sloan-Kettering Cancer Center, 1375 York Ave., New York, NY, 10021
Cancer; 48(5):1245-1250 1981

A retrospective study of 25 patients with malignant lymphoma who had osteonecrosis of either the femoral or humeral head(s) was undertaken. The common factor present among all patients was the administration of intermittent steroid-containing combination chemotherapy. Seventeen Hodgkin's disease patients received chemotherapy predominantly consisting of an alkylating agent, vincristine, procarbazine, and moderate amounts of prednisone. The non-Hodgkin's lymphoma patients were on various moderate dosage steroid-containing protocols, except three who received prolonged high-dose steroid-containing chemotherapy regimens. Sixteen of the 17 Hodgkin's disease patients and five of the eight non-Hodgkin's lymphoma patients received radiotherapy to the bones that subsequently developed osteonecrosis. Two of the three non-Hodgkin's lymphoma patients who were not irradiated were treated with high-dose steroid-containing chemotherapy regimens. Symptoms developed in patients 12 mo and 32 mo after completion of chemotherapy and radiotherapy, respectively. Osteonecrosis was a long-term complication of treatment between 1970 and 1979 and occurred in 1.6% of the Hodgkin's disease and 0.12% of the non-Hodgkin's lymphoma patients treated. The authors conclude that the patients at highest risk for this complication are those who receive both radiotherapy to the affected bone(s) and intermittent steroid-containing multiple drug chemotherapy. (Author abstract) (24 Refs)

MALIGNANT LYMPHOMA: DIAGNOSIS AND STAGING

13. CENTRAL NERVOUS SYSTEM LEUKEMIA AND LYMPHOMA: COMPUTED TOMOGRAPHIC MANIFESTATIONS.

Pagani JJ, Libshitz HI, Wallace S, Hayman LA
Dept. Diagnostic Radiology, Univ. Texas System Cancer Center, M. D. Anderson Hosp. and Tumor Inst., 6723 Bertner, Houston, TX, 77030
AJNR; 2(5):397-403 1981

Experience with the intracranial computed tomographic (CT) manifestations of leukemic and lymphomatous masses in 405 patients (245 with leukemia, 148 systemic non-Hodgkin's lymphoma, 12 systemic Hodgkin's lymphoma) is reviewed. After contrast enhancement, 31 patients had intracerebral lesions; the CT abnormalities in these patients were correlated with the underlying malignancy, cerebrospinal fluid cytology, and treatment. All CT studies were performed with an EMI 1010 scanner either immediately after 40 g iv iodine or 1 hr after high dose (80 g iodine) contrast infusion. Abnormalities in 24/245 patients with leukemia included leukemic masses (8), hemorrhage (9), abscesse (2) , and 5 other abnormalities including one each acoustic neuroma, astrocytoma, and methotrexate leukoencephalopathy. The only CT abnormality in 160 lymphoma patients was a tumor mass in 7. CT was normal in 374 patients including 148 with meningeal disease diagnosed by cerebrospinal fluid cytologic examination. Malignant masses before treatment appeared isodense or of greater density with varying amounts of edema. Worsening was indicated by increase in the size or number of masses. After radiation therapy and chemotherapy, a central low density region with an enhancing rim developed. The differential diagnosis of the various abnormalities is discussed. (24 Refs)

14. ANGIOGRAPHY AND COMPUTED TOMOGRAPHY IN THE DIAGNOSIS OF PRIMARY LYMPHOMA OF THE BRAIN.

Tallroth K, Katevuo K, Holsti L, Andersson U
Dept. Radiology, Meilahti Hosp., SF-00290 Helsinki, Finland
Clin Radiol; 32(4):383-388 1981

Three patients with primary lymphomas of the brain are presented. The angiographic and computed tomographic (CT) appearances resembled the few cases reported previously. In all three cases angiography showed avascular tumors with little vessel displacement or involvement whereas the CT scans showed large strongly and homogeneously enhancing tumor masses. Neither method alone gives pathognomonic appearances, but taken together angiography and CT should suggest the diagnosis of this rare tumor. (Author abstract) (21 Refs)

15. STAGING LAPAROTOMY IN CUTANEOUS T-CELL DISEASE.

Doyle JA, Winkelmann RK
Dept. Dermatology, Mayo Clinic and Mayo Foundation, Rochester, MN, 55905
Arch Dermatol; 117(9):543-546 1981

Staging laparotomy performed in 13 patients with various forms of cutaneous T-cell disease (mycosis fungoides, Sezary syndrome, cutaneous lymphoma, atrophic parapsoriasis, and alopecia mucinosa) showed evidence of visceral or lymph node involvement in three (23%) patients; in two of these patients, noninvasive investigations and staging procedures did not disclose any abnormalities. All three patients were alive after a mean follow-up period of 3 1/2 yr. In the 10 patients with normal findings at laparotomy, the presence of intra-abdominal lymphoma was suggested in six by noninvasive staging procedures (lymphangiogram, spleen or liver-spleen scan, and computerized tomographic scan of the abdomen). Five of these 10 patients died; 4 of the 5 patients died after relentless progression of the disease and visceral involvement. Staging laparotomy may have a role in the management of cutaneous T-cell disease because noninvasive investigations may be poor indicators of the presence or absence of intra-abdominal disease. The course of these patients, even those in whom laparotomies did not show any abnormalities, emphasizes the progressive potential of cutaneous T-cell disease. (Author abstract) (21 Refs)

16. GASTRO INTESTINAL LYMPHOMAS: A RETROSPECTIVE ANALYSIS.

Saksena A, Shankur R, Rajvanshi VS
Dept. Pathology, G. S. V. M. Medical Coll., Kanpur, India
Indian J Cancer; 18(2):123-127 1981

Between 1969 and 1979, 48 lymphomas of the gastrointestinal (GI) tract were identified out of 426 cases of lymphomas. Most of the 48 GI lymphomas were of the non-Hodgkin's group (79.17%) with 20.83% in the Hodgkin's disease group. Approx half of the cases were restricted to the second and third decades; only 12.5% presented after 50 yr. All age groups showed a male preponderance. Most patients presented with signs of intestinal obstruction, progressively increasing abdominal lump, and loose motions. Wt loss and anorexia were common. The primary sites were the ileum (35.4%), colon (20.8%) and only one case (2.08%) occurred in the duodenum. Grossly, approx 60% showed a diffuse infiltration of the intestinal wall with flat, greyish-white, plaque-like lesions and concomitant loss of mucosal pattern. The draining mesenteric lymph nodes were enlarged in 75%. Follicular hyperplasia with a sinus reaction of lymph nodes was found in half of the cases, and the specific lesion in the other half. Hodgkin's disease was the mixed cellularity type, while the non-Hodgkin's lymphomas were lymphocytic lymphoma, poorly differentiated type (33.3%) and lymphocytic lymphoma, intermediate differentiation (22.9%). The clinicopathologic findings and their relation to possible etiological factors were discussed. (17 Refs)

17. MALIGNANT LYMPHOMA SUPERVENING IN CHRONIC LYMPHOCYTIC LEUKEMIA AND RELATED DISORDERS. RICHTER'S SYNDROME: A STUDY OF 25 CASES.

Harousseau JL, Flandrin G, Tricot G, Brouet JC, Seligmann M, Bernard J
(c/o Flandrin) Laboratoire de Cytologie, Institut de Recherche sur les Leucemies et les Maladies du Sang, Hopital Saint-Louis, 75475-Paris Cedex 10, France
Cancer; 48(6):1302-1308 1981

Richter's syndrome (RS) has been defined as 'histiocytic' lymphoma (HL) or Hodgkin's disease (HD) supervening in the course of chronic lymphocytic leukemia (CLL) and related disorders. The clinical, histologic, and immunologic findings in 25 cases (11 women, 14 men) of RS are presented. The initial diagnosis was CLL in 19 cases, diffuse well-differentiated lymphocytic lymphoma in 2 cases, and Waldenstrom's macroglobulinemia in 4 cases. The interval between the initial diagnosis and that of RS ranged from 0 (2 cases) to 120 mo (median 49 mo). At the time of diagnosis of RS, the initial lymphoproliferative disorder was an apparent complete remission in only two cases. The lymphoma was disseminated in at least 18 cases. The overall median survival was 4 mo, but complete remission was achieved in six cases and has been maintained for 15 to 77 mo. In four of these six cases, the RS was localized. The histologic diagnosis of HD was made in only two cases. In the other 23 cases the diagnosis was HL, but in 5 of these cases, the proliferation was heterogeneous and was considered as an early aspect of HL. Immunologic studies of lymph node cell suspensions were performed in seven cases. In all cases, the B-lymphocytic origin of the lymphoma cells could be ascertained. Detailed studies in four cases showed that lymphoma cells carried SIg of the same isotype and light chain type as that of SIg detected on CLL cells or of monoclonal serum Ig. In these cases, the lymphoma was actually related to the initial B-cell chronic lymphoid disease. (Author abstract) (33 Refs)

18. MALIGNANT LYMPHOMA, INTERMEDIATE LYMPHOCYTIC TYPE: A CLINICOPATHOLOGIC STUDY OF 42 CASES.

Weisenburger DD, Nathwani BN, Diamond LW, Winberg CD, Rappaport H
(c/o Rappaport), City of Hope Natl. Medical Center, Duarte, CA, 91010
Cancer; 48(6):1415-1425 1981

A clinicopathologic analysis of 42 cases of non-Hodgkin's *lymphoma of the intermediate lymphocytic type (ILL) having* morphologic features between those of well-differentiated (WDLL) and poorly differentiated lymphocytic lymphoma (PDLL) is presented. In lymph node sections, ILL was characterized by a diffuse proliferation consisting predominantly of small lymphoid cells with slightly irregular or indented nuclei. A mixture of lymphoid cells with entirely round nuclei and lymphoid cells with angulated and cleaved nuclei was also present, but each of these two cell populations did not comprise more than 30% of the total. The median age of the patients was 65 yr, and the male-to-female ratio was 5:1. Generalized lymphadenopathy was evident in 74% of the patients, and B symptoms were presented in 36%. Peripheral blood involvement was present at the onset of disease in 21% of the patients, and the bone marrow was involved by lymphoma in 76% of those examined. Five percent of the patients had Stage I disease, 24% had Stage III disease, and 71% had Stage IV disease. Ninety-three percent of the patients received multiagent chemotherapy and 41% achieved a complete remission. The overall median survival was 31 mo. Clinical features which appeared to influence survival adversely included the presence of B symptoms ($p = 0.007$), age greater than 70 yr ($p = 0.09$), and absolute lymphocyte count above 5,000/mm3 ($p = 0.05$), and anemia ($p = 0.09$). Achievement of a complete remission influenced survival favorably ($p = 0.02$). Pathologic features which appeared to influence survival included sinus obliteration, which had an adverse effect ($p = 0.05$), and the presence of residual germinal centers which had a favorable effect ($p = 0.06$). Patients with 0-5 mitoses/10 high power fields (HPF) had a significantly longer survival than those with more than 20 mitoses/10 HPF ($p = 0.02$), while those with 6-20 mitoses/10 HPF had an intermediate survival. The clinical and pathological features of patients with ILL suggest that this entity is closely related to PDLL and should be distinguished from WDLL. (Author abstract) (35 Refs)

19. NON-HODGKIN'S LYMPHOMA OF LARGE MULTILOBULATED CELL TYPE. A CLINICOPATHOLOGIC STUDY OF TEN CASES.

Weinberg DS, Pinkus GS
(c/o Pinkus) Dept. Pathology, Brigham and Women's Hosp., 75 Francis St., Boston, MA, 02115
Am J Clin Pathol; 76(2):190-196 1981

Recently, the authors described a distinct variant of T-cell lymphoma characterized morphologically by large multilobated nuclei, and clinically by a predilection for extranodal sites and a favorable prognosis. In a retrospective study of 75 cases of 'histiocytic' lymphomas observed during a 13-yr period, 10 additional cases of this unusual variant of non-Hodgkin's lymphoma were identified. Features similar to those of the initial group of cases included a predominant extranodal distribution, particularly involving skin, sc tissue, and bone, and a favorable response to therapy. However, the retrospective cases differed in that systemic symptoms were infrequent and gonadal involvement was not observed. Recognition of this morphologically distinct subtype of non-Hodgkin's lymphoma is of diagnostic, therapeutic, and prognostic significance. (Author abstract) (24 Refs)

20. BURKITT'S LYMPHOMA IN JAPAN: CLINICOPATHOLOGICAL FEATURES OF TWENTY-TWO PATIENTS.

Abe K, Sato T
Dept. Pediatrics, Hokkaido Univ. Sch. Medicine, Kitaku, Sapporo 060, Japan
Tohoku J Exp Med; 134(3):289-293 1981

Twenty-two cases of Burkitt's lymphoma in Japan were reviewed and their clinicopathological features were compared with those reported in African and American patients. There were 14 males, 8 females; aged 1-29 yr, mean age 9.5 yr. Most (19) were between 1 and 15 yr old. Five were Stage I, eight Stage II, six Stage III, and three Stage IV. Sites of involvement included the facial bone (20), abdomen (8), exophthalmus (5), cranial neuropathy (3), paraplegia (1), testes (1), and breast (1). The bone marrow was involved and leukemic transformation was observed in seven patients during the course of their disease. One of 17 patients tested for antibody titers to Epstein-Barr virus had a significantly elevated level. Serum lactic dehydrogenase levels were lower in patients with localized disease than those with advanced disease. The mean survival was 3.8 mo after diagnosis and no significant differences were found between the stage of disease and survival. (16 Refs)

21. GRANULOCYTIC SARCOMA: A CLINICOPATHOLOGIC STUDY OF 61 BIOPSIED CASES.

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Cancer; 48(6):1426-1437 1981

Granulocytic sarcoma is an uncommon tumor composed of granulocytic precursor cells. Because it occurs in a variety of clinical settings and because the tumor cells are primitive it is frequently unrecognized during life. This presentation details the authors' experience with 61 biopsy-proven granulocytic sarcomas. The patient age range was from 2 to 81 yr (mean 48 yr). In eight patients the tumors were multiple. Most common sites of involvement were bone, periosteum, soft tissue, lymph node and skin. Twenty-two tumors occurred in 15 patients with no known disease, 26 occurred in 24 patients with a known myeloproliferative disorder, and 13 occurred in 11 patients with proven acute myeloid leukemia. Thirteen of the 15 patients with no known disease developed acute leukemia in from 1 to 49 mo after the biopsy of their tumors (mean 10 mo). Most tumors occurring in patients with a known myeloproliferative disorder were associated with blast crisis. The authors' cases displayed a morphologic range from well-differentiated to those tumors that displayed virtually no evidence of differentiation by conventional microscopy. It was therefore not surprising that most tumors were originally diagnosed as lymphoma. Chloro-acetate esterase (CAE) stains were performed on 56 tumors and 47 were studied with the antilysozyme immunoperoxidase technique. Fifty-six of the 57 specimens studied by either technique were positive. Antilysozyme immunoperoxidase stains were particularly useful in confirming the diagnosis. (Author abstract) (51 Refs)

22. FINE NEEDLE ASPIRATION BIOPSY: A USEFUL TOOL IN TUMOR CYTOGENETICS WITH SPECIAL REFERENCE TO MALIGNANT LYMPHOMAS.

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Cancer Genet Cytogenet; 4(1):53-60 1981

A method for chromosome analysis of malignant cells by means of fine needle aspiration biopsy has been developed. The method has some obvious advantages compared to conventional surgical biopsy. During a 1-yr period 25 consecutive non-Hodgkin, non-Burkitt lymphoma biopsies from 19 patients have been studied. In 14 out of 21 lymph node biopsies chromosome analysis was successful; whereas, 4 biopsies of sc lymphomas were unsuccessful. (Author abstract) (5 Refs)

23. CYTOGENETIC FINDINGS IN T-ZONE LYMPHOMA.

Godde-Salz E, Schwarze EW, Stein H, Lennert K, Grote W
Dept. Human Genetics, Univ. Kiel, Schwanenweg, D-2300 Kiel, W. Germany
J Cancer Res Clin Oncol; 101(1):81-89 1981

Histologic, immunologic, and cytogenetic findings are reported for five non-Hodgkin's lymphomas that fulfilled the diagnostic criteria of T-zone lymphoma; ie, they contained all the T-region components of lymphoid tissue and also B-region remnants. The patients, aged 64-77 yr, included two women and three men. In 4/5 cases, the lymph node architecture was completely effaced, with the exception of the residual B areas (follicles). The B cells were identified immunologically as the nonneoplastic cells, and the cells that formed rosettes with sheep RBC were found to be the tumor cells. The chromosome analyses revealed abnormal clones as well as normal mitoses in four cases. Structural rearrangements involved chromosomes 1, 2, 3, 4, 14, and Y. Some tumors showed the loss of chromosomes 3, 5, 6, or 13 and some a gain of chromosomes 3 and 9. There was a high frequency of structural and numerical aberrations in chromosome 3, but a low frequency of 14q markers in one case. The number of patients was too small to determine whether this pattern is specific for the T-zone lymphomas. (21 Refs)

24. IMMUNOLOGIC MARKERS IN THE DIFFERENTIAL DIAGNOSIS OF NON-HODGKIN'S LYMPHOMAS.

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Inst. Pathology, Univ. Kiel, Hospitalstrasse 42, D-2300 Kiel, W. Germany
J Cancer Res Clin Oncol; 101(1):29-42 1981

To improve the Kiel classification of non-Hodgkin's lymphomas (NHLs), 250 NHLs were analyzed for surface markers and enzyme phenotype. B-cell chronic lymphocytic leukemias (CLLs) were characterized by a predominance of complement (C) 3d receptors over C3b receptors, and a high percentage of RBC receptors. Four of five T-cell CLLs showed acid esterase activity but lacked IgG-Fc receptors; the reverse was true of the fifth case. Prolymphocytic leukemias exhibited a high percentage of surface immunoglobulin (SIg)-positive cells and large numbers of C3b and IgG-FC receptor-positive cells. Hairy cell leukemias resembled the prolymphocytic leukemias except for the absence of C3 receptors. T-zone lymphomas contained both T and B cells; the T cells formed rosettes with sheep RBC only at 4 C, and they were identified morphologically as the neoplastic cells. The three types of lymphomas derived from germinal center cells expressed nearly equal numbers of C3b and C3d receptors a low percentage of IgG-Fc receptors. Centrocytic lymphomas, in in contrast to centroblastic-centrocytic (CC) lymphomas, had a high proportion of cells with SIg and C3 receptors and few or no T cells and cells rosetting with mouse RBC. The marker profiles of centroblastic lymphomas and lymphoplasmacytic subtype of lymphoplasmatic/cytoid lymphomas (IP immnocytomas) resembled that of CC lymphomas. The lymphoplasmacytoid IP immunocytoma subtype had the same markers as B-cell CLLs, but the marker profile of the polymorphic subtype was not similar to any other pattern. Burkitt's lymphoblastic lymphomas were characterized by large amounts of SIg and the absence of all other markers. Four types of T-cell lymphoblastic leukemias were distinguished on the basis of the presence or absence of C3 receptors, sheep RBC receptors, and acid phosphatase, or acid esterase. Of nine immunoblastic lymphomas, eight were the B-cell type (SIg+) and one was the T-cell type (sheep RBC receptors). (19 Refs)

25. TERMINAL DEOXYNUCLEOTIDYL TRANSFERASE-CONTAINING CELLS IN PERIPHERAL BLOOD: IMPLICATIONS FOR THE SURVEILLANCE OF PATIENTS WITH LYMPHOBLASTIC LEUKEMIA OR LYMPHOMA IN REMISSION.

Froehlich TW, Buchanan GR, Cornet JM, Sartain PA, Smith RG
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Blood; 58(2):214-220 1981

An indirect immunofluorescence assay was used to quantitate TdT-containing (TdT+) cells in the mononuclear WBC fraction of peripheral blood from normal subjects and patients with acute lymphoblastic leukemia (ALL) and lymphoblastic lymphoma (LL). In normal children (10) and adults (10), 0.036% +-0.014% (mean +- SD) and 0.030% +-0.015% TdT+ cells were found. In peripheral bloods from 10 children receiving chemotherapy for tumors other than ALL or LL, 0.040% +-0.039% TdT+ cells were found. Serial determinations were performed on 15 patients with ALL or LL who were in clinical remission. Eight of these patients remained in continuous remission and always had fewer than 0.11% TdT+ cells in their peripheral blood. Three patients who developed systemic relapse were found to have progressively rising numbers of TdT+ cells in their peripheral blood prior to clinical evidence of relapse. All three of these patients had greater than 0.1% TdT+ cells in their peripheral blood from 3 to 8 wk prior to clinical relapse. In three other patients, localized extramedullary relapse developed, but no trend was found on serial TdT determinations. Thus, the indirect immunofluorescence assay for TdT detects a small population of cells in normal peripheral blood. In patients with ALL, progressive increases above this normal level were associated with subsequent bone marrow relapse. (Author abstract) (17 Refs)

26. ENZYME POLYMORPHISM IN THE CLASSIFICATION OF HUMAN MALIGNANT LYMPHOMA.

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Inst. Pathology, Univ. Kiel, Hospitalstrasse 42, D-2300 Kiel, W. Germany
J Cancer Res Clin Oncol; 101(1):53-57 1981

Protein-related acid phosphate (AP) activity and the enzyme isoelecric focusing pattern (IEF) were studied in normal B lymphocytes and B lymphocytes from patients with B-cell chronic lymphocytic leukemia (B-CLL: 9 cases), lymphoplasmacytic/lymphoplasmacytoid lymphoma (IC: 28 cases), centroblastic/centrocytic follicular lymphoma (CB: 10 cases) or plasmacytoma (PC: 8 cases). The normal B lymphocytes showed weak AP activity (1.8 milliunits/10(7) cells). The neoplastic lymphocytes showed a stepwise increase of AP activity from B-CCL to PC. B-CLL and CB/CC lymphocytes shared the basic IEF pattern of normal lymphocytes; ie, 12 bands between pH 6.3 and 3.85. In contrast, IC lymphocytes showed two additional isoenzymes (between the cathodal region A and the intermediate region B) and PC lymphocytes demonstrated five additional bands (between the intermediate region B and the anodal region). These results suggested that AP isoenzyme patterns can be used for the identification of different cell lines and the classification of their neoplastic derivatives. (12 Refs)

MALIGNANT LYMPHOMA: CLINICAL IMMUNOLOGY AND IMMUNOTHERAPY

27. EXPRESSION OF COMMON ACUTE LYMPHOBLASTIC LEUKEMIA ANTIGEN (CALLA) BY LYMPHOMAS OF B-CELL AND T-CELL LINEAGE.

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Blood; 58(3):648-652 1981

Previous studies have demonstrated that the common acute lymphoblastic leukemia antigen (CALLA) is expressed by leukemic cells from approx 80% of patients with non-T-cell ALL and 30%-50% of patients with chronic myelocytic leukemia in blast crisis. A small number of normal bone marrow and fetal liver cells also express CALLA, but the functional role of this molecule is unknown. In the present study, we have used a monoclonal antibody (J5) specific for CALLA to study the expression of this antigen in non- Hodgkin's lymphomas. Within the B-cell lymphomas, it was found that CALLA was expressed by almost all Burkitt's and nodular poorly differentiated lymphocytic lymphomas. Within the T-cell lymphomas, CALLA was expressed in 40% of patients with lymphoblastic lymphoma. Three of three Burkitt's lymphoma cell lines and three of eight T-lymphoblast cell lines were also found to express CALLA. Normal spleen, lymph node, and thymus cells were not reactive with J5 antibody. These findings indicate that expression of CALLA is not limited to relatively undifferentiated leukemic lymphoblasts but also occurs in more differentiated lymphoid malignancies. However, normal differentiated lymphoid cells in lymph node, spleen, and thymus, which have a phenotype similar to that of lymphoma cells, do not appear to express CALLA. (Author abstract) (26 Refs)

28. SCANNING IMMUNO-ELECTRON MICROSCOPY OF HUMAN LEUKAEMIA AND LYMPHOMA CELLS: A COMPARATIVE STUDY OF TECHNIQUES USING IMMUNOLATEX SPHERES AS MARKERS.

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Dept. Hematology, Hadassah Univ. Hosp., Jerusalem, Isreal
J Microsc; 123(2):189-199 1981

Scanning immuno-electron microscopic (SIEM) techniques were used to identify human leukemia-lymphoma cells, using monodispersed polystyrene (latex) beads conjugated to specific antisera by glutaraldehyde (immunolatex spheres). A variety of cells of known origin were studied in an attempt to detect surface antigenic components. The antisera were usually immunoglobulin fractions and were prepared against human thymus-derived (T) cells, common type acute lymphoblastic leukemia (C/ALL) cells, and surface immunoglobulin (sIgG)-bearing cells. Several types of experiments were carried out: (1) to determine whether it is essential to neutralize fixed samples with glycine before the addition of immunolatex, (2) to test the immunospecificity of the antisera conjugated to the latex spheres, using both fixed and unfixed cells, and (3) to ascertain the surface morphology of human leukemia-lymphoma cells positively labeled with the specific antisera. Glycine treatment was essential for detecting specific antigenic sites on the cell surface by SIEM. The immunospecificity of the heteroantisera was adequate; insignificant non-specific attachment and cross reactivity were seen. SIEM is a useful technique for ultrastructural studies of the human leukemia-lymphoma cells and is a potentially useful tool in their identification. (32 Refs)

29. ANTI-IA-REACTIVE CELLS IN MYCOSIS FUNGOIDES: A STUDY OF SKIN BIOPSIES, SINGLE EPIDERMAL CELLS AND CIRCULATING T LYMPHOCYTES.

Tjernlund UM, Scheynius A, Kabelitz D, Klareskog L
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Acta Derm Venereol (Stockh); 61(4):291-301 1981

Skin sections, epidermal cells in suspension and circulating T lymphocytes were investigated for the presence of Ia-like antigens in a group of patients with the cutaneous T-cell lymphoma mycosis fungoides (MF) and in healthy controls. Highly purified anti-Ia antibodies were used in indirect immunofluorescence, indirect peroxidase and peroxidase-antiperoxidase techniques. Allogeneic and peroxidase-antiperoxidase techniques. Allogeneic and autologous mixed leukocyte reaction tests with epidermal cells from MF lesions as stimulator cells were also performed The majority of the dermal lymphohistiocytes and mononuclear cells in the epidermal Pautrier microabscesses expressed Ia-like antigens. So also did a greater proportion of circulating T lymphocytes than in the controls. In some MF patients a high percentage of single epidermal cells of non-lymphoid character also reacted with the antibodies. The possible significance of the present findings for the pathogenesis of MF is discussed. (Author abstract) (30 Refs)

30. IMMUNOHISTOLOGICAL ANALYSIS OF HUMAN LYMPHOID TISSUE BY DOUBLE IMMUNOENZYMATIC LABELLING.

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J Cancer Res Clin Oncol; 101(1):13-22 1981

A double immunoenzymatic labeling technique for the visualization of pairs of antigens on human lymphoid tissue is described along with its application to paraffin-embedded and cryostat sections of normal or neoplastic tissues. The technique is based on the reaction of rabbit anti-alkaline phosphatase (AP) with an AP substrate and the reaction of goat, sheep, or, preferably, rabbit and mouse monoclonal antibodies with a peroxidase substrate. Cells containing both immunoglobulin (Ig) kappa and lambda chains, cells containing Ig and albumin, and cells containing IgM and IgG were detected in double-labeled paraffin sections. The cells that stained for both Ig light chain classes included Reed-Sternberg and Hodgkin's cells and the giant cells in non-Hodgkin's lymphomas. The double IgM/IgG cells were rare in nonneoplastic tissue and were not found in any of the greater than 100 non-Hodgkin's lymphomas studied. The double staining of cryostat sections with monoclonal antibodies enabled the simultaneous visualization of a variety of antigen pairs (eg, T-cell antigens and IgD). The greater preservation of antigenic reaction in the cryostat sections (compared with the paraffin sections) coupled with the wide range of antigens potentially detectable with monoclonal antibodies suggested that future studies in this area will add greatly to the knowledge of the human lymphoid system. (19 Refs)

31. HETEROGENEITY OF LYMPHOBLASTIC MALIGNANCIES IN CHILDREN.

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J Cancer Res Clin Oncol; 101(1):23-27 1981

Lymphocyte surface markers were studied in 6 children with null cell lymphoblastic lymphomas (LLs), 16 with T cell LLs, and 15 children with B cell LLS. The null cell tumors showed a phenotype of acute lymphoblastic leukemia (ALL) antigen+ Ia antigen+ and terminal deoxyribonucleotidyl transferase (TdT)+. The T cell tumors showed three major phenotypic subgroups: HTLA+, E rosette-, TdT+, and occasional ALL cells (prethymic phenotype); E rosette+, HTLA+, and Tdt+ (thymic cortical phenotype); and E rosette+-, HTLA+, complement 3d+, and TdT- (fetal thymic phenotype). Most B cell tumors had the phenotype of surface IgM immunoglobulins with or without cytoplasmic IgM, and which may express ALL antigen. A small group of B cell tumors expressed the surface IgM and complement 3d phenotype reminiscent of adult follicular lymphoma. The phenotypic heterogeneity found in these children indicated that further studies will be needed before an adequate histologic and phenotype classification of these malignancies can be developed. (no Refs)

32. NATURAL ANTIBODIES TO THE HUMAN T CELL LYMPHOMA VIRUS IN PATIENTS WITH CUTANEOUS T CELL LYMPHOMA.

Posner LE, Robert-Guroff M, Kalyanaraman VS, Poiesz BJ, Ruscetti FW, Fossieck B, Bunn PA, Minna JD, Gallo RC
Lab. Tumor Cell Biology, NIH, Bethesda, MD, 20205
J Exp Med; 154(2):333-346 1981

Serum samples were obtained from patients with cutaneous T cell lymphoma (CTCL) and leukemia, and from 55 normal random donors. Retroviruses HTLV-CR (grown in HUT 102 cells) and HTLV-MB, isolated from patients CR and MB, respectively, were used, along with several other retroviruses. The sera were screened for the presence of natural antibody to HTLV-CR, using a solid-phase radioimmunoassay. Sera from patient CR and one other patient reacted specifically with proteins of HTLV-CR. CR serum also reacted with HTLV-MB proteins. Solid-phase immunocompetition and competition radioimmunoprecipitation assays demonstrated the specificity for HTLV-CR proteins. Patient CR antibodies were directed against viral core proteins with mol wt of 24,000 and 19,000, as shown by radioimmunoprecipitation analysis. Some reactivities to other animal retroviruses, including the baboon endogenous virus, simian sarcoma virus, feline leukemia virus, and gibbon ape leukemia virus, were demonstrated. These reactivities apparently were not virus-specific, but related to cellular antigen contamination of viral preparations or to antigens in fetal calf serum. The results indicate for the first time a specific antibody reaction to a retrovirus in humans. (38 Refs)

33. AN IMMUNOCYTOCHEMICAL STUDY OF NON-HODGKIN'S LYMPHOMAS.

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Cancer; 48(4):915-922 1981

Lymph node specimens obtained intraoperatively and/or at autopsy from 89 patients with non-Hodgkin's lymphoma were studied immunohistochemically. The peroxidase anti-peroxidase (PAP) technique was used for detecting monoclonal cytoplasmic immunoglobulin (CIg) and for determining the classes and types of immunoglobulins in the tumors. Following rigid criteria, monoclonal CIg was demonstrated in 4 (16%) of 25 cases of nodular, poorly differentiated lymphocytic lymphoma (NPDL); in 3 (14%) of 21 cases of diffuse, poorly differentiated lymphocytic lymphoma (DPDL); and in 13 (30%) of 43 cases of diffuse histiocytic lymphoma (DH). Of the four NPDL patients, two had the Mkappa, one the Akappa, and one the lambda chain type. Of the three DPDL patients, one had the Mkappa, one the Gkappa, and one the lambda chain type. Of the 13 DH patients, 5 had the Mkappa, 4 the Akappa, 1 the GMkappa, 1 the Alambda, 1 the Glambda, and 1 the kappa chain type. In two DH patients negative for cytoplasmic immunoglobulins, cytoplasmic lysozyme was present, indicating the histiomonocytic nature of the tumor cells. There was no significant difference between the overall survival rates for the DH patients with or without monoclonal CIg. In all three types of lymphoma studied, we encountered many patients (67%) who had tumor cell populations without demonstrable CIg and few patients (11%) with polyclonal CIg. There are several possible reasons why many of the patients were PAP-negative and why some had polyclonal cell populations. The PAP method may be useful in establishing the monoclonal nature of neoplastic lymphoid cell populations. (Author abstract) (49 Refs)

34. THE ANALYSIS OF LYMPHOID SUBPOPULATIONS IN NORMAL AND MALIGNANT TISSUES BY IMMUNOFLUORESCENE TECHNIQUE.

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J Cancer Res Clin Oncol; 101(1):1-11 1981

Antibodies labeled with fluorescein isothiocyanate and tetraethylrhodamine isothiocyanate were used to analyze the cellular composition of normal lymphoid tissues and 40 non-Hodgkin's lymphomas by immunofluorescence (IF) in frozen tissue sections. The antisera tested included conventional reagents to immunoglobulin classes, human thymocyte (T cell) and Ia-like antigens, and monoclonal antibodies including the OKT antibodies that react with T-cell subpopulations. The IF technique was found to give an accurate analysis of the normal and malignant cells and to yield information complementary to conventional histology. In normal tissues, the combination of antisera to Ia-like antigens and T lymphocytes made it possible to identify reticular cells corresponding to interdigating (ID) cells in peripheral lymphoid tissue. Membrane antigens on ID cells, lamina propria macrophages, and lymphocytes were labeled with a monoclonal antibody to human WBC antigen. Reagent combinations that simultaneously recognized T and B lymphoid cells revealed intriguing variations in the proportion and location of the T cells in B-lymphomas. In some patients, large proportions of T lymphocytes and blasts were clearly seen in close contact with B cells of variable size. Further studies with antibodies to T-cell subsets of inducer and suppressor functions should reveal the clinical significance of these findings. (39 Refs)

35. BINDING OF PEANUT LECTIN TO GERMINAL-CENTRE CELLS: A MARKER FOR B-CELL SUBSETS OF FOLLICULAR LYMPHOMA?

Rose ML, Habeshaw JA, Kennedy R, Sloane J, Wiltshaw E, Davies AJ

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Br J Cancer; 44(1):68-74 1981

The binding of horseradish-peroxidase-labeled peanut lectin (HRP-PNL) to cryostat sections of tonsil, lymphoma lymph nodes, reactive lymph nodes and miscellaneous tumors demonstrated that PNL binds selectively to lymphocytes in germinal centers. Lymph nodes from 21 patients with non-Hodgkin's lymphomas were phenotyped as cell suspensions for PNL binding, and the following surface markers: E rosetting, C3d, SIg, OK markers of T-cell subsets, Ig heavy-chain and light-chain classes. There was a positive correlation between PNL binding and cells with SIg and C3d receptors. 4/5 cases of centroblastic/centrocytic follicular lymphoma had a PNL+ SIg+ C3d+ phenotype. Both cases of centroblastic/centrocytic diffuse lymphoma were PNL-. There was no correlation between PNL binding and heavy- or light-chain Ig class. PNL binding and presence of C3d receptors were not always positively correlated, indicating that follicular cells may be either PNL+ SIg+ C3d+ or PNL+ SIg+ C3d-. The binding pattern of PNL to one case of thymic hyperplasia and two cases of malignant lymphoma lymphoblastic T type suggested that some but not all cortical thymocytes bind PNL. (Author abstract) (9 Refs)

MALIGNANT LYMPHOMA: CHEMOTHERAPY

36. TREATMENT OF RECURRENT LYMPHOMAS WITH VINCRISTINE, BCNU, DOXORUBICIN, AND PREDNISONE (VBAP): A SOUTHWEST ONCOLOGY GROUP STUDY.

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Cancer Treat Rep; 65(7/8):611-614 1981

Chemotherapy with vincristine, carmustine (BCNU), doxorubicin, and prednisone (VBAP) was administered to 75 patients with malignant lymphoma, including both Hodgkin's disease and non-Hodgkin's lymphoma. All patients had prior chemotherapy with or without radiation therapy. Remissions were achieved in 41% of all patients, with only minor toxicity. The median duration of remission for Hodgkin's disease and non-Hodgkin's lymphoma was 51 and 22 wk, respectively. The median survival for all patients was 34 wk. The VBAP program is effective palliative chemotherapy for advanced malignant lymphoma. (Author abstract) (11 Refs)

37. THE TREATMENT OF ADVANCED STAGE FAVORABLE HISTOLOGY NON-HODGKIN'S LYMPHOMA: A PRELIMINARY REPORT OF A RANDOMIZED TRIAL COMPARING SINGLE AGENT CHEMOTHERAPY, COMBINATION CHEMOTHERAPY, AND WHOLE BODY IRRADIATION.

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Blood; 58(3):592-598 1981

Between 1975 and 1978, 51 patients with favorable histology non-Hodgkin's lymphomas, pathologic Stage III-IV, were treated prospectively on a randomized treatment protocol. Treatment options were single alkylating agent chemotherapy, combination chemotherapy with cyclophosphamide, vincristine, and prednisone (CVP), or fractionated whole body irradiation followed by low dose involved field irradiation. The median follow-up interval in this group of patients is now 41 mo. Actuarial survival is excellent, 84% at 4 yr for the entire group, with similar survival observed for each of the three treatment options. Initial complete remission rates (64%, 88%, and 71%) were not significantly different in the three treatment arms. Frequent relapse after initial remission induction was noted, however, with a freedom from relapse at 4 yr of only 25%. The toxicities of the three therapies were acceptable. Acute complications of therapy were most numerous in the group of patients treated with CVP; however, long-term hematologic depression was most commonly observed in patients treated with whole body irradiation. In general hematologic complications were more frequent among patients who had marrow involvement and intact spleens at the time of initial therapy. The relationship of this study to other clinical trials in the management of patients with advanced stage favorable histology lymphomas and its implications for future clinical trials are discussed. (Author abstract) (36 Refs)

38. IMMEDIATE RESULTS OF NEW POLYCHEMOTHERAPEUTIC PROTOCOL FOR NON-HODGKIN'S LYMPHOMAS.

Tolmacheva EL, Arkhipova NE, Tentsova IA, Chernova MK, Burova GF, Polianskaia AM, Khomchenovskii EI, Fainshtein FE

First Hematologic Clinic, Central Inst. Hematology and Blood Transfusion, Moscow, USSR

Sov Med; (6):82-83 1981

The therapeutic efficacy of CPP protocol (cyclophosphamide: 800-1,000 mg, iv, on days 1 and 8; pafencil: 75 mg/day, po, for 14 days; and prednisolone: 60 mg/day, po, for 14 days) was studied in 69 patients with non-Hodgkin's lymphoma. The group included 9 patients with Stage II-III and 60 with Stage IV-V; 27.2% had the lymphoblastic variant, 48.2% the prolymphocytic variant, 1.8% the lymphoplasmacytic variant, 18.7% the lymphocytic variant, and 4.1% the histiocytic or undifferentiated variant. At least three courses of polychemotherapy were required to achieve a remission. Objective improvement was recorded in 100% of the patients; 26.7% entered a complete remission. Av duration of remission after the CPP protocol was 14 mo. (8 Refs) (In RUS)

39. ADRENAL RESPONSE TO SERIAL COSYNTROPIN STIMULATION AFTER REPEATED HIGH-DOSE PREDNISONE ADMINISTRATION IN PATIENTS WITH LYMPHOMA.

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Cancer Treat Rep; 65(7/8):563-566 1981

To determine if repeated courses of high-dose prednisone given to patients with lymphoma as part of multiple-drug chemotherapy programs would lead to progressive adrenal suppression, serial cosyntropin stimulation tests were performed. Four patients with diffuse histiocytic lymphoma (group 1) received prednisone for 5 days every 3 wk for five courses, and five patients with Hodgkin's disease (group 2) received prednisone for 14 days every 4 wk for six courses. Testing was done on day 1 of each treatment course prior to the administration of therapy and after the final course of chemotherapy. In group 1 patients, there was no evidence of adrenal suppression after any of the courses of prednisone. The plasma cortisol increments after cosyntropin injection were also normal. In the group 2 patients, significant depression of basal plasma cortisol concentrations was observed after the first and fifth courses of prednisone, compared to the pretreatment values. The depression reflected the previous course of prednisone administration only and was not progressive with subsequent courses. The plasma cortisol increments after cosyntropin injection were normal despite depressed basal plasma cortisol levels. (Author abstract) (12 Refs)

MALIGNANT LYMPHOMA: RADIOTHERAPY

40. MEGAVOLT ELECTRON IRRADIATION FOR LOCALIZED MYCOSIS FUNGOIDES.

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Acta Radiol Oncol Radiat Phys Biol; 20(2):71-74 1981

A retrospective analysis was carried out to evaluate the effectiveness of small field megavolt electron irradiation for localized mycosis fungoides. Only local field electron beam therapy was employed for limited disease reserving total skin electron irradiation for multiple lesions or diffuse disease covering at least 25% of the entire body surface. Of the 14 patients with limited disease treated between 1964 and 1973 with the local field technique, 10 patients (71%) are alive without evidence of disease at a minimum of 5 yr. In contrast, of 200 patients with extensive cutaneous disease who received total skin electron irradiation, only 16 (8%) were considered cured. It is concluded that early localized mycosis fungoides is potentially curable, and that limited field electron beam therapy with a relatively low total dose is adequate to obtain excellent response. (Author abstract) (17 Refs)

MALIGNANT LYMPHOMA: MULTIMODAL THERAPY

41. TREATMENT OF NON-HODGKIN'S LYMPHOMA WITH MARROW TRANSPLANTATION IN IDENTICAL TWINS.

Appelbaum FR, Fefer A, Cheever MA, Buckner CD, Geenberg PD, Kaplan HG, Storb R, Thomas ED

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Blood; 58(3):509-513 1981

Eight patients with disseminated non-Hodgkin's lymphoma who failed conventional combination chemotherapy were treated with high-dose chemotherapy, a supralethal dose of total-body irradiation, and a bone marrow transplant from a normal identical twin. Seven patients experienced complete remissions. Four of the seven patients (two with diffuse poorly differentiated lymphocytic lymphoma, one with composite lymphoma, and one with diffuse moderately well differentiated lymphocytic lymphoma) remain in complete unmaintained remission 12-126 mo from transplantation. One patient relapsed after 10 mo but was retreated and is alive in unmaintained complete remission 73 mo from transplantation. One patient died of Pseudomonas pneumonia while in complete remission and one patient relapsed and died of progressive lymphoma. These results demonstrate that intensive chemoradiotherapy and twin marrow transplantation can induce frequent and enduring remissions in patients with disseminated non-Hodgkin's lymphoma who have failed conventional therapy. (Author abstract) (20 Refs)

MALIGNANT LYMPHOMA: CASE REPORTS

42. FIVE PATIENTS WITH MALIGNANT LYMPHOMA ORIGINATING IN THE BREAST (MEETING ABSTRACT).

Horikoshi N, Inagaki J, Inoue K, Okabe K, Aiba K, Domyo M, Nagata T, Ogawa M, Sakamoto G, Takano Y

Dept. Chemotherapy, Cancer Inst. Hosp., Toshima-ku, Tokyo 170, Japan

Nippon Monaikei Gakkai Kaishi; 21(1):96 1981

Five female patients who had malignant lymphoma originating in the breast were seen between 1966 and 1980. They were 19 to 55 yr old and had a mastectomy. The initial site was both breasts for one patient, and the right breast for the others. Relapse occurred in the other breast in two patients 5 mo, and 5 yr and 4 mo after surgery. Metastasis to the regional lymph nodes was observed at the time of surgery in three patients. Histologically, the patients all had non-Hodgkin's disease. According to Rappaport's classification, four patients had diffuse histiocytic (DH) and the other had diffuse poorly differentiated lymphocytic lymphoma (DPDL). According to the Lymphoma Study Group of Japan classification, all of the lymphomas were diffuse type; three were large-cell type and two were medium-sized cell type. None of the patients received post operative radiation therapy, but two patients were given chemotherapy BEMP (bleo mycin + cyclophosphamide + 6-mercaptoprine + prednisolone) and VCP (vincristine + cyclophosphamide + prednisolone). One patient died 3 wk after surgery, and two died 6 mo after surgery. As of the end of 1980, one patient with histologically DPDL was still alive 45 mo after surgery, and the other was alive 69 mo after the first surgery and 5 mo after the second surgery for relapse in the left breast. (no Refs) (In JPN)

MALIGNANT LYMPHOMA: SELECTED REPORTS ON ETIOLOGY AND EPIDEMIOLOGY

43. INITIAL EVENT IN MYCOSIS FUNGOIDES OF THE SKIN IS VIRAL INFECTION OF EPIDERMAL LANGERHANS CELLS.

MacKie RM
Dept. Dermatology, Anderson Coll. Building, 56 Dumbarton Road, Glasgow G11 6NU, Scotland
Lancet; 2(8241):283-285 1981

Malignant transformation of T lymphocytes has been proposed as the primary event in the development of cutaneous lymphoid infiltrates of the mycosis fungoides (MF) type. The alternative hypothesis of initial viral infection of the immunologically competent epidermal Langerhans cell leading to a defect in Langerhans cell/lymphocyte interaction and subsequent faulty lymphocyte recirculation is proposed. In only a proportion of these cases does a true T-cell lymphoma develop. (Author abstract) (23 Refs)

MALIGNANT LYMPHOMA: SELECTED PRE-CLINICAL STUDIES

44. TUMOR STEM CELLS ON AGAR: INITIAL DATA.

Ludwig C, Ludwig R, Obrecht JP
(c/o Obrecht) Onkologische Abteilung, Departement fur innere Medizin, Universitat Basel (Kantonsspital), CH-4031 Basel, Switzerland
Schweiz Med Wochenschr; 111(36):1313-1318 1981

Hamburger and Salmon have recently developed an in vitro assay for human tumor stem cells which permits formation of colonies of human solid tumors and lymphomas in soft agar. In 50 patients with solid tumors or lymphomas studied by us, tumor colonies grew from effusions and biopsies in 75% of patients (17 of 21) with histologically or cytologically involved specimens. Lymphoid colony growth was obtained in about 25% of specimens (5 of 19) including malignant lymphomas. Conversely, no colony growth was observed in 10 cases where the biopsies or effusions were histologically or cytologically negative. The effect of various conditioned media on tumor growth in agar was investigated. Colony formation of solid tumors was promoted to an especially marked extent by cell-free malignant effusions. This assay yields satisfactory results in solid tumors and appears useful for investigation of different cytotoxic effects of anticancer drugs on the survival of human tumor colony-forming cells. (Author abstract) (14 Refs) (In GER)

45. HUMAN HEMATOPOIETIC TUMORS IN NUDE MICE.

Sordillo PP, Hansen H, Jhanwar SC, Beck J, Lieberman P, Helson L
Memorial Sloan-Kettering Cancer Center, Cornell Univ. Sch. Medicine, 1275 York Ave., New York, NY, 10021
Exp Cell Biol; 49(5):256-266 1981

Despite the difficulty in establishing human hematopoietic tumors in nude mice, four human lymphomas were successfully heterotransplanted and passaged serially in our laboratory. Additional immunosuppression with chemotherapy, whole-body radiation or splenectomy was not required for establishment of these tumors. All four of these tumors were of the non-Hodgkin's lymphoma type. In each case the tumors in the nude mice were histologically identical to the biopsy specimens from the patient in whom they were derived. Attempts to transplant tumors from 17 patients with Hodgkin's disease or 4 patients with immunoblastic lymphadenopathy were unsuccessful. Tumors from two patients with chronic myelogenous leukemia and one with hairy cell leukemia could be grown in nude mice conditioned with whole-body radiation or cytosine arabinoside, but these tumors could not be passaged to other nude mice. Cell surface markers were determined on the four serially passaged lymphomas. These surface markers were similar to the markers on the original tumors, even after long periods of mouse-to-mouse passage. In one patient with fevers, night sweats and mediastinal mass in whom a diagnosis had not been made after several biopsies, examination of tumor tissue that had been transplanted from the patient to the nude mouse clearly established the diagnosis of lymphoma. (Author abstract) (24 Refs)

46. GOAT LYMPHOSARCOMA FROM BOVINE LEUKEMIA VIRUS.

Olson C, Kettmann R, Burney A, Kaja R
Dept. Veterinary Science, Univ. Wisconsin-Madison, 1655 Linden Drive, Madison, WI, 53706
JNCI; 67(3):671-675 1981

A goat given inoculations of sheep lymphocytes from cultures that produced bovine leukemia virus (BLV) died 8 yr later with lymphosarcoma. The tumors were located in various lymph nodes, the mesentery, omentum, body wall, and retrobulbar tissues. The BLV had been cultured from lymphocytes during the 1st yr after the goat's infection, and persisting BLV antibodies could be demonstrated when the animal was 7.5 yr old. BLV provirus was identified by molecular hybridization in the DNA of the goat tumors at the above five locations. The tumors were similar to those found in lymphosarcoma of the adult bovine type (BLV associated). Normal goat liver, normal calf thymus, and calf-type lymphosarcoma (not BLV associated) served as negative controls. Our serologic, histologic, and molecular hybridization studies are evidence that the lymphosarcoma was induced by BLV. (Author abstract) (14 Refs)

MALIGNANT LYMPHOMA: REVIEWS

47. BURKITT'S LYMPHOMA.

Ziegler JL
NCI, Bethesda, MD, 20205
N Engl J Med; 305(13):735-745 1981

Recent developments that have added to the understanding of biologic, etiologic, and clinical aspects of Burkitt's lymphoma (BL) are reviewed. Detailed discussions present the immunology of malignant lymphoma, and etiology, clinical features, staging, treatment, and immunology of BL. BL now ranks with the dozen neoplasms that can be cured by drugs alone. BL is also the leading candidate for a virus-induced human tumor; studies of this association led to the discovery of Epstein-Barr virus as the cause of infectious mononucleosis. Experimental and clinical examination of BL have greatly expanded the study of immunobiology and tumor immunology. (121 Refs) **LYMPHOMAS; Diagnosis, Treatment**

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• **MALIGNANT LYMPHOMA: SELECTED PRE-CLINICAL STUDIES** **40-42**

HODGKIN'S DISEASE: DIAGNOSIS AND STAGING

1. IMPORTANCE OF NUCLEAR MEDICAL METHODS IN MONITORED SERIES OF PATIENTS WITH HODGKIN'S DISEASE.

Dienstbier Z, Masopust J, Bechyne M, Foltynova V, Kocmerzevska H
Inst. Biophysics and Nuclear Medicine, Faculty of General Medicine, Charles Univ., Salmovska 3, 12000 Prague, Czechoslovakia
Radiobiol Radiother (Berl); 22(3):359-365 1981

Seventy-three patients with malignant lymphogranuloma (Hodgkin's disease) were monitored between 1970 and 1980. A total of 714 radionuclide examinations and 831 verifications by other means were performed in the course of diagnosis, determination of the extent of disease, follow-up of therapy, and diagnosis of relapse. Methods used included isotope indirect lymphography using 198Au colloid, 67Ga scintigraphy, liver scintigraphy using 99m-Tc sulfur colloid, 198Au sulfide colloid, or 113m-In colloid, pulmonary vascular perfusion using 99m-Tc or 131I, bone scanning with 99m-Tc pyrophosphate or 85 SrCl2, bone marrow scintigraphy with 99m-Tc sulfur colloid or 111In, radioisotope renography, or spleen scintigraphy with 99m-Tc-labeled erythrocytes. Results of isotopic studies were compared with x-ray, biochemical, and hematological studies done not more than 3 mo before or after the isotopic studies. The highest correlation with studies not using isotopes was obtained with 67Ga scanning (84.7%). The lowest was obtained with liver scintigraphy (63.5%). Isotopic lymphography, because of its relative simplicity, proved useful for diagnosis and detection of relapse. Bone scintigraphy proved useful for detecting metastatic tumor involvement. Liver scintigraphy results were often nonspecific. (15 Refs)

2. CLINICAL SIGNIFICANCE OF HEPATIC ISOENZYME OF LACTATE DEHYDROGENASE LDH IN THE DIFFERENTIAL DIAGNOSIS OF MALIGNANT LYMPHOMA.

Damle SR, Karkhanis VC, Nadkarni JS, Shetty PA, Jussawalla DJ
Immuno-Biochemical Lab., Dept. Chemotherapy, Tata Memorial Hosp., Parel, Bombay 400 012, India
Indian J Cancer; 18(3):185-187 1981

Serum levels of lactate dehydrogenase-5 isoenzyme (LDH-5) were studied for clinical significance in 164 patients. Cases included over 100 with Hodgkin's disease (HD) and over 50 with non-Hodgkin's lymphoma (NHL). Total LDH activity was assayed. LDH was then fractionated into isoenzymes. LDH-5 activity was significantly raised in HD patients without liver involvement (mean value 76 +-46 IU) compared with normal controls (mean value 12 IU). LDH-5 levels correlated with the clinical stage of disease. LDH-5 activity (mean value 29 +-16.7 IU) was at or near control levels in NHL patients. LDH activity was raised in 18% of poorly differentiated NHL patients having liver involvement (mean value 58 +-13.4 IU). Distribution of other LDH isoenzymes agreed with previous reports of raised LDH activity in malignant conditions. Results suggest LDH-5 activity as a diagnostic indicator in HD patients. Increase in LDH-5 in NHL patients seems to be due to liver involvement, rather than disease activity. (12 Refs)

3. LAPAROSPLENECTOMY IN HODGKIN'S DISEASE.

Colombo L, Colombo P, Bellini F, Lunghi C
Istituto di Clinica Chirurgica Generale e Terapia Chirurgica, Universita di Pavia, Pavia, Italy
Minerva Chir; 36(11):777-786 1981

Laparosplenectomy performed during 1973-1979 on 102 patients (53 male, 49 female, av age 32 yr) with Hodgkin's disease is assessed. Indications for using the procedure are reviewed with respect to progress of the disease and histologic type; findings made during laparosplenectomy are compared with preoperative diagnostic data based mainly on lymphography, hepatosplenic scintiscan, and functional exploration of the liver. Four conclusions are drawn: (1) isotopic and functional tests are insufficient and unreliable, (2) precision in criteria for intraoperative location of splenic Hodgkin sites is lacking, (3) discrepancy exists between histologic lymphonodal results and lymphography, and (4) primary subdiaphragmatic splenic involvement has high incidence. Laparosplenectomy is found valuable for ascertaining real spread of the disease and for allowing selection of more precise and suitable therapy. Removal of the spleen may protect the liver from disease invasion and prevent the need for irradiation. (17 Refs) (In ITA)

HODGKIN'S DISEASE: CLINICAL IMMUNOLOGY AND IMMUNOTHERAPY

4. SERUM IGD IN HODGKIN'S DISEASE.

Gobbi PG, Merlini G, Lattanzio G, Perugini S
Istituto di Patologia Medica Ia, Universita di Pavia, Policlinico San Matteo, 27100 Pavia, Italy
Haematologica (Pavia); 66(1):35-45 1981

Serum IgD levels were measured in 56 Hodgkin's disease (HD) patients (34 male, 22 female; 13-63 yr old). Mean value of serum IgD was significantly higher in HD patients than in normal subjects. In HD patients with lymphocyte predominance, the IgD levels appeared normal and were significantly lower than in patients with the other three histological types of HD. Among the latter, only nodular sclerosis and mixed cellularity groups exhibited IgD levels significantly higher than normal; the difference in lymphocyte depletion subjects was not significant. In patients with stages other than Stage I HD, IgD levels were significantly higher than normal; no significant difference was observed between these different stages. No significant relationship was found between IgD level and sex, spleen involvement or splenectomy, or form and length of treatment. A fair correlation was observed between serum IgD level and therapeutic response: IgD decreased significantly with remission but not with partial or non-response. Serum IgD may reflect the immune reaction to tumor-associated antigens of the Hodgkin-Sternberg cells, and be of value in monitoring response to treatment. (18 Refs)

5. IMMUNOLOGICAL STUDY ON HODGKIN'S DISEASE WITH SPECIAL REFERENCE TO LYMPHOCYTE INHIBITOR.

Chen YC, Deng JS
Dept. Internal Medicine, Natl. Taiwan Univ. Hosp., Taipei, Republic of China
J Formosan Med Assoc; 80(1):55-67 1981

The characteristic T-cell anergy of Hodgkin's disease (HD) was studied in 5 HD patients and compared with that observed in 8 patients with non-Hodgkin's lymphoma (NHL) and 28 healthy controls. The presence of a serum factor in HD patients which is capable of suppressing phytohemagglutinin (PHA) blastogenesis of T-cells from normal controls and HD patients was examined. Lymphocytopenia was found in 2/5 HD patients but not in NHL patients. The percentages of T and B lymphocytes were similar in all three groups. Positive reaction to id purified protein derivative of tuberculin test occurred in 1/5 HD patients, 3/8 NHL patients, and 11/16 controls. The PHA transformation index (TI) was markedly depressed in HD. Differences in PHA TI were not significant between HD and NHL patients, although the PHA TIs of both groups differed significantly from those of controls. Serum IgG, IgM, and IgA levels were within normal ranges for the HD patients. Data implied that some factor was present in the sera of HD patients which was capable of suppressing the transformation response of normal lymphocytes to PHA. The effect of this serum inhibitory factor on the TI of different lymphocyte sources was studied. The lymphocytes from the three groups were incubated in 20% fetal calf serum (FCS) and 20% HD serum (HS) from HD Cases A, C, and D, and the ratios of PHA TI in HS to PHA TI in FCS were measured. The ratios were much lower in HD. In 3/4 HD patients tested with HS from Case D (HS-D), a PHA TI of less than 1 (suppression) was observed. This finding contrasted with those of NHL patients and normal subjects whose PHA-TI were always over 1 (stimulation) when HS-D was added. The significance of this factor is discussed. (41 Refs)

HODGKIN'S DISEASE: CHEMOTHERAPY

6. LONG-TERM FOLLOW-UP OF OVARIAN FUNCTION IN WOMEN TREATED WITH MOPP CHEMOTHERAPY FOR HODGKIN'S DISEASE.

Schilsky RL, Sherins RJ, Hubbard SM, Wesley MN, Young RC, DeVita VT
Building 10, Room 12N226, Bethesda, MD, 20205
Am J Med; 71(4):552-556 1981

Twenty-seven women previously treated with MOPP (mechlorethamine, vincristine, procarbazine, prednisone) chemotherapy were evaluated to determine the status of ovarian function. All patients had completed therapy a median of 9 yr earlier and had a median age of 30 yr at the time of evaluation. Persistent amenorrhea has occurred in 11 of 24 patients (46%) treated with MOPP alone or MOPP plus radiation excluding the pelvis. Of patients with amenorrhea, 89% were older than age 25 at the time of treatment. In contrast, 80% of patients younger than age 25 at treatment continue to menstruate regularly. The time from diagnosis to amenorrhea was significantly shorter in the older patients ($p = 0.001$). Evaluation of serum gonadotropin and estradiol levels confirms ovarian failure as the cause of amenorrhea in all patients. Overall, these 27 patients have borne 13 normal children subsequent to chemotherapy. This long-term follow-up study demonstrates that chemotherapy-induced ovarian failure is age-related, that ovarian failure is often gradual in onset following the completion of chemotherapy and that, to date, the children born of women treated with this chemotherapy regimen appear to be entirely normal. (Author abstract) (17 Refs)

7. COMBINATION CHEMOTHERAPY FOR STAGE IV HODGKIN'S DISEASE (REPORT NO 14).

Goldman JM
(c/o G. Hudson) Dept. Oncology, Middlesex Hosp., London, W1, England
Clin Radiol; 32(5):531-536 1981

From 1970 to 1975 patients with Stage IV Hodgkin's disease randomized for treatment in the British National Lymphoma Investigation were treated either with MOPP (nitrogen mustard, vincristine, procarbazine and prednisolone) or MOP (the same combination without prednisone). The incidence of complete remission was significantly higher for patients treated with MOPP than for those who received MOP (69 vs 36%, p less than 0.01) and the duration of survival also favored the former group. From 1976 to 1979 patients with Stage IV disease were treated either with MOPP or with MOPP plus bleomycin at low dosage (B-MOPP); the incidence of complete remission was not significantly different in the two groups of patients (52 vs 65%) and a trend in survival favoring those treated by B-MOPP was not significant. The present trial is a comparison of MOPP with the same combination in which chlorambucil has been substituted for nitrogen mustard (LOPP). A proportion of those patients who achieved complete remission after treatment with MOPP or B-MOPP was randomized for maintenance for 6 mo with CVB combination (lomustine, vinblastine and bleomycin). No advantage could be discerned for patients 'maintained' in this way. (Author abstract) (21 Refs)

8. PROTECTION OF OVARIAN FUNCTION BY ORAL CONTRACEPTIVES IN WOMEN RECEIVING CHEMOTHERAPY FOR HODGKIN'S DISEASE.

Chapman RM, Sutcliffe SB
Dept. Hematology, Walter Reed Army Inst. of Res., Washington, DC, 20012
Blood; 58(4):849-851 1981

It has been reported by us and by others that after chemotherapy for Hodgkin's disease the ovary contains fewer than five primordial and primary follicles per 5 x 5 mm biopsy section. In young women this is associated with premature menopause. We report here that before treatment the tissue contains 18-55 such follicles per biopsy section. When women took combination oral contraceptives throughout the course of MVPP therapy (nitrogen mustard, vinblastine, procarbazine and prednisone), the post-treatment ovarian biopsy tissue had more than 20 follicles per histologic section. Normal menses were established in the five women who discontinued oral contraceptives at the end of MVPP therapy, and one of them is now pregnant. (Author abstract) (11 Refs)

9. USE OF VM-26 (EPIIODOPHILOTOXIN) IN THE TREATMENT OF ACUTE LEUKEMIAS AND LYMPHOMAS IN ADULTS.

Kondrat'eva NA, Gershanovich ML, Kondrat'ev VB, Lebedev VN, Vygovskaia IaI, Iavorkovskii LI
Dept. Cooperative Studies in Clinical Oncology, Cancer Res. Center, Moscow, USSR
Probl Gematol Pereliv Krovi; 26(7):10-14 1981

The results of the cooperative clinical trials of VM-26 (epiiodophilotoxin) in 80 patients (40 men, 40 women, 15-70 yr old) Hodgkin's disease (HD), lymphosarcoma (LS), and acute leukemia (AL) are reported. Of 80 patients, 53 received short, 5-day, courses of VM-26 (30 mg/square meter, iv) with 10-day intervals between the courses, and 27 received long courses (40 mg/square meter, iv, 2x/wk, for 3-4 wk). Complete and partial remissions were recorded in 18.6% and 7.5% of the patients with HD, 21.4% and 35.8% of the patients with LS, and in 2.6% and 10.2% of the patients with AL. Subjective improvement was achieved in 33.3% of the patients with HD, 21.4% of the patients with LS, and in 12.8% of the patients with AL. Side-effects were nausea and vomiting (55.5% in HD, 42.8% in LS, and 12.8% in AL), marked fatigue (18.5%, 7.1%, and 5.1%, respectively), and leukopenia (44.4%, 21.4%, and 25.6%, respectively). (11 Refs) (In RUS)

HODGKIN'S DISEASE: RADIOTHERAPY

10. THE PLACE OF RADIOTHERAPY IN THE MANAGEMENT OF LOCALISED HODGKIN'S DISEASE (REPORT NO 11).

Hope-Stone HF
(c/o G. Hudson) Dept. Oncology, Middlesex Hosp., London, W1, England
Clin Radiol; 32(5):519-526 1981

This report reviews the experience of the BNLI in managing localized Hodgkin's disease, since the BNLI began in February 1970. The original problem investigated by this study was the evaluation of 'prophylactic' irradiation treating adjacent apparently unaffected regions, as opposed to radiation directed to only the affected regions of the body. Because lower half Hodgkin's disease is uncommon, the study was confined to patients presenting with upper half disease, with 'B' symptoms. Diagnostic laparotomy and splenectomy was not considered to be a mandatory investigation and at the commencement of the study was recommended by only two collaborators. By the completion of the study the majority of collaborators were recommending this procedure routinely. This study therefore includes two additional subgroups of patients with Stages I, IIA (upper half) Hodgkin's disease. In the laparotomized group of patients a 10-yr survival rate of almost 95% with either 'local' or 'prophylactic' irradiation suggests that wide field irradiation (including total nodal irradiation) is not essential in the cure of apparently localized Stages I, IIA (upper half) Hodgkin's disease, provided the extent of the disease has been accurately determined by previous investigation. In those patients treated with strictly localized (as opposed to 'prophylactic') irradiation, relapses in adjacent unirradiated regions have been completely controlled by additional treatment, usually irradiation, and none have died of Hodgkin's disease. (Author abstract) (11 Refs)

11. RADIOISOTOPIC STUDY OF SOME ORGANS AFTER RADIOTHERAPY ON THE UPPER ABDOMEN.

Romanini A, Galli G, D'Errico G, Carlesimo M, De Renzis C
Istituto di Radiologia, Universita Cattolica - Policlinico A. Gemelli, Via della Pineta Sacchetti, 526, 00168 Roma, Italy
Radiol Med (Torino); 67(10):757-761 1981

Morphological and functional changes in liver and kidney were studied: before upper abdominal radiotherapy, immediately after, and followed up at different time intervals to evaluate observed alterations. Twenty five patients 17-55 yr old (13 females, 12 males; 12 in Stage II and 13 in Stage III) with Hodgkin's disease underwent clinical examination and surgery. All patients received approx 45 Gray radiotherapy. Patients underwent nephrography, renal plasmatic flux, glomerular filtration, liver scintigraphy with 99Tcm colloids, liver function with 131I-Bengal rose, and pancreas scintigraphy. The experimental results indicated possible left liver lobe damage in younger patients and transitory impairment of some renal function (glomerular filtration reduction). (49 Refs) (In ITA)

HODGKIN'S DISEASE: MULTIMODAL THERAPY

12. COMBINED THERAPY OF HODGKIN'S DISEASE.

Vorob'ev AI, Fokina NT, Brilliant MD, Fil'kova EM

Dept. Hematology, Central Inst. Advanced Training for Physicians, Moscow, USSR

Probl Gematol Pereliv Krovi; 26(8):3-7 1981

The efficacy of combined therapy was evaluated in 147 patients (71 men, 76 women; 11-63 yr old) with Hodgkin's disease (HD). Treatment included splenectomy, polychemotherapy according to MOPP (mustine + oncovin + prednisone + procarbazine) or COPP (cyclophosphamide + oncovin + prednisone + procarbazine) regimens, and radical radiotherapy (4,500-5,000 rads to the involved lymph nodes and 3,500-4,000 rads to the regions of potential metastatic spread). Complete remission of 3-70-mo duration was recorded in 78% of the patients treated with COPP regimen; MOPP regimen provided complete remission of 6-72-mo duration in 90% of the patients. Recurrences were recorded in 17% of the patients treated with COPP and in 14% treated with MOPP. An overall 5-yr survival rate was 90.2% (73% in the patients with Stage IV HD). (14 Refs) (In RUS)

13. RADIOTHERAPY OR CHEMOTHERAPY AS THE INITIAL TREATMENT FOR STAGE IIIA HODGKIN'S DISEASE (REPORT NO 13).

Strickland P

(c/o G. Hudson) Dept. Oncology, Middlesex Hosp., London, W1, England

Clin Radiol; 32(5):527-530 1981

This report describes three comparative studies of treatment methods in patients with Stage IIIA Hodgkin's disease in whom the extent of disease had been confirmed by a diagnostic laparotomy. The first trial (1970-75) compared TNI with MOPP. The recurrence-free survival curve for patients treated with TNI was significantly better than that for those treated with MOPP at 4 yr, but the survival rate of the two cohorts was identical, presumably because of good salvage treatment. The second study (1975-80) compared TNI with TNI followed by LOPP. Initially the addition of LOPP appeared to improve the disease-free survival rate but at 3 yr no difference was apparent between the two treatment groups. The third (1980-present) study divides patients into those with and those without splenic involvement. Retrospective analysis of all patients included in the BNLI with Stage IIIA Hodgkin's disease confirmed by laparotomy and treated initially by TNI shows that splenic involvement does not influence the survival but decreases the relapse-free survival rate, making additional treatment with MOPP necessary in 75% of long-term survivors. In the current study, patients without splenic involvement are treated with TNI whereas those with splenic involvement are treated initially with chemotherapy, randomizing between MOPP and LOPP. (Author abstract) (4 Refs)

HODGKIN'S DISEASE: SELECTED REPORTS ON ETIOLOGY AND EPIDEMIOLOGY

14. EPSTEIN-BARR VIRUS INFECTION AND NEOPLASIA.

Sprinkle PM, Veltri RW
Dept. Otolaryngology, West Virginia Univ., Morgantown, WV
Otolaryngol Head Neck Surg; 89(4):542-544 1981

Conclusive serological data of activation of Epstein-Barr virus (EBV) is reported showing persistently elevated early antigen (EA) titers prior to and following malignant transformation in a 6-yr-old boy. Heterophil-negative EBV disease characterized by lymphadenopathy and recurrent tonsillitis developed in the child 1 mo after his sister died with heterophil-negative infectious mononucleosis. Epstein-Barr nuclear antigen (EBNA) and EA were detected in many B-lymphocytes present in each of the same tissue specimens. One yr later, rebiopsy of the cervical nodes revealed typical Hodgkin's disease. EBNA and EA were found in hilar and celiac lymph nodes as well as in splenic lymphocytes. Serum antibody study demonstrated a 1:640 EA and 1:2,560 viral capsid antigen-IgG specific antibody to their EBV-coded antigens. Before and after the diagnosis of Hodgkin's disease, however, the patient's EA titers were persistently elevated and remained so. The child was alive with a poor prognosis after multiple chemotherapy courses and two courses of radiotherapy. The child's mother died in the interim with undifferentiated lymphoma. (16 Refs)

15. SEROEPIDEMIOLOGIC STUDIES IN HODGKIN'S DISEASE.

Kokosha LV, Lapin BA, Lebedev VN, Danilova NV, Arshba NN, Bologov VN
Lab. Experimental Oncology, Inst. Experimental Pathology and Therapy, Sukhumi, USSR
Probl Gematol Pereliv Krovi; 26(8):12-16 1981

To evaluate the possibility of horizontal transmission of Epstein-Barr virus (EBV), antibodies against capsid antigen of EBV were determined in 109 patients with Hodgkin's disease (HD) and in 67 relatives of 46 patients. High titers of antivirus antibodies were recorded in 70% of the patients with HD. The highest titers were recorded in the patients with lymphoid exhaustion (1:256, compared with 1:97 in lymphoid predominance and mixed cell variant, and 1:49 in nodular sclerosis). The titers of antibodies against EBV antigen in the relatives were significantly greater that that in healthy donors (1:69 and 1:6, respectively). (34 Refs) (In RUS)

MALIGNANT LYMPHOMA: DIAGNOSIS AND STAGING

16. USE OF INTRAVENOUS LIPOSOLUBLE CONTRAST MATERIAL FOR THE EXAMINATION OF THE LIVER AND SPLEEN IN LYMPHOMA.

Vermess M, Bernardino ME, Doppman JL, Fisher RI, Thomas JL, Velasquez WS, Fuller LM, Russo A
Diagnostic Radiology Dept., Building 10, Room 6S211, NIH, Clinical Center, Bethesda, MD, 20205
J Comput Assist Tomogr; 5(5):709-713 1981

An experimental contrast material has been developed that, after iv injection, selectively opacifies the spleen and liver on computed tomography (CT). The contrast material contains iodinated ester of poppy seed oil in an emulsified form. Clinical trials were recently initiated to test the value of this contrast agent in Hodgkin's and non-Hodgkin's lymphomas. We present here two of our initial patients in whom we found lesions in the spleen or liver following the infusion of the experimental contrast material that were not visualized on the precontrast and urographic contrast material enhanced CT scans. (Author abstract) (13 Refs)

17. CONTRAST MEDIA IN COMPUTED TOMOGRAPHY OF THE MEDIASTINUM AND THE LUNG.

Wegener OH, Claussen CD, Thurn P, Frommhold W, Lackner K, Felix R, Zur Nedden D, Blumenfeld SM, Lipton MJ, Zeitler E, Kormano M, Baert A, Young SW
Radiologische Abteilung, Free Univ. Berlin, West Berlin, W. Germany
Excerpta Med Int Congr Ser; 561:214-225 1981

Evaluation of the mediastinum by computed tomography should begin with a native scan to eliminate questionable findings from other procedures. A contrast medium infusion technique, in which dose is dependent on duration of the scan, should be used to evaluate mediastinal processes for vascular relationships or lymphoma. Bolus injection should be used for localized processes. Findings and conclusions are discussed. (no Refs)

18. THE CURRENT STATUS OF SPLENIC COMPUTED TOMOGRAPHY IN PATIENTS WITH LYMPHOMA.

Harell GS
Div. Diagnostic Radiology, Dept. Radiology, Stanford Univ. Medical Sch., Stanford, CA
Excerpta Med Int Congr Ser; 561:237-242 1981

Results of examination of 25 patients with Hodgkin's disease or non-Hodgkin lymphoma by computed tomography (CT) and other diagnostic procedures were analyzed. CT produced a large number of false negative results. Bolus injection of water-soluble contrast media had varying degrees of success. Nondynamic CT has not been successful in detection of splenic involvement by lymphoma. (18 Refs)

19. INTRACRANIAL MALIGNANT LYMPHOMA: CLINICAL VIEW AND PATHOLOGICAL AND IMMUNOLOGICAL EXAMINATION (MEETING ABSTRACT).

Shibuya N, Kobayashi T, Inoue I, Kageyama N, Sakano K, Yoshida J, Hirota T, Tajima M, Suchi T
Dept. Neurosurgery, Nagoya Univ., Sch. Medicine, Showa-ku, Nagoya 466, Japan
Program and Abstracts of the 22nd Annual Meeting of Japanese Society of Neurology held in Kumamoto, Japan, 20-22 May, 1981. Japanese Society of Neurology, Tokyo 113, Japan, 282 pp., 1981.

Fifteen patients with intracranial malignant lymphoma were seen during the past 7 yr. They were from 6 mo to 70 yr old with an av age of 42.1 yr. The male to female ratio was 9:6. The initial site was the cerebrum, cerebellum and brain stem for seven, four and two patients, respectively. The length of the period from onset to diagnosis was from 1 to 16 mo (av 5 mo). Surgery was performed by direct intracranial approach on 14 patients. Radiation therapy was given to 14 patients and chemotherapy to 4. Steroids and depressors for brain pressure were given to seven patients for 1 to 9 mo before diagnosis, and temporary remission of the symptoms occurred. Computed tomography (CT) was performed on 13 patients, 10 of whom had CT before and after irradiation. The tumors could be diagnosed and the effect of therapy determined by CT. Eleven patients died 3 mo to 2 yr (av 10.5 mo) after therapy, the prognosis for younger and older persons being the worst. Four patients were still alive 2 mo to 2 yr and 1 mo (av 8.4 mo) after therapy. All of the patients had pathologically diffuse type lymphoma, determined by hematoxylin-eosin staining (the Lymphoma Study Group (LSG) classification proposed by Suchi et al). Ten had large cell (6 immunoblastic), 2 mixed and 1 each medium-sized cell and lymphoblastic lymphoma. All of the lymphomas except for the lymphoblastic lymphoma were considered to be of B-cell origin. B-cell markers were confirmed in two recent patients by enzyme histochemical examination of a fresh tumor tissue obtained during surgery. (no Refs) (In JPN)

20. FREQUENCY OF MALIGNANT NON-HODGKIN'S LYMPHOMAS IN BIOPSY MATERIAL. A RETROSPECTIVE STUDY.

Rudiger KD, Wockel W
Institut Allgemeine Pathologie und Pathologische Anatomie, Medizinischen Akademie, Nordhauser Strasse 74, DDR-5060 Erfurt, E. Germany
Zentralbl Allg Pathol; 125(3):191-198 1981

The biopsy material of the Institute of Pathology of the Medical Academy of Erfu rt, GDR, from January 1967 to February 1978 has been reinvestigated for malignant non-Hodgkin's lymphomas which were reclassified according to the Kiel classification. We observed 122 (72.6%) low grade malignant lymphomas and 46 (27.4%) high grade malignant lymphomas. Seventeen cases remained unclassifiable. The median age ranged between 47.6 yr (lymphoblastic malignant lymphoma) and 65.8 yr (centrocytic malignant lymphoma). The sex ratio shows a predominance of males for all types of low grade malignant lymphomas. Only the immunoblastic malignant lymphoma in the group of high grade malignant lymphomas has a predominance in females. The survival of patients with high grade malignant lymphomas shows a good correspondence to the data given in the literature, whereas patients suffering from low grade malignant lymphomas have a distinctly worse prognosis in our material in comparison to literature data. (Author abstract) (17 Refs) (In GER)

21. MORPHOLOGIC CRITERIA FOR THE DIFFERENTIATION OF FOLLICULAR LYMPHOMA FROM FLORID REACTIVE FOLLICULAR HYPERPLASIA: A STUDY OF 80 CASES.

Nathwani BN, Winberg CD, Diamond LW, Bearman RM, Kim H
City of Hope Natl. Medical Center, Duarte, CA, 91010
Cancer; 48(8):1794-1806 1981

A study was made of 80 patients whose lymph nodes were characterized by the presence of follicles throughout the lymph node. The patients were divided into two groups on the basis of the clinical follow-up information. The first group consisted of 20 patients who were alive and disease-free at the end of 5 yr without therapy. The patients in this group were classified as having florid reactive follicular hyperplasia (FRFH). The second group of 60 patients had progressive, recurrent, clinically active disease and were classified as having follicular lymphoma (FL). Forty-six were dead of active disease, and 14 were alive with disease. Various morphologic parameters were evaluated at low and high magnification, and statistical comparisons were made between FRFH and FL. Although several criteria were helpful in distinguishing FRFH from FL, the single most valuable criterion was the type of pattern encountered. Follicles of variable size and shape lying adjacent to each other throughout the lymph node without or with very little intervening tissue are diagnostic of FL. This pattern was evident in 85% of the FL cases, but was not observed in any of the cases of FRFH. (Author abstract) (21 Refs)

22. THE PROGNOSTIC VALUE OF PRESENTING SERUM LDH IN NON-HODGKIN LYMPHOMA.

Ridgway D, Smiley S, Neerhout RC

Dept. Pediatrics, Univ. Oregon Health Sciences Center, 3181 S. W. Sam Jackson Park Road, Portland, OR, 97201

J Pediatr; 99(4):611-613 1981

Serum lactate dehydrogenase (LDH) and disease course were reviewed in 23 consecutive pediatric patients (26 mo-17 yr old) with non-Hodgkin's lymphoma (10 Burkitt, 3 diffuse histiocytic, 8 diffuse lymphoblastic, and 2 undifferentiated non-Burkitt lymphomas) seen over a 48-mo period. Of the 23 patients, 22 were treated with multi-drug chemotherapy. The serum LDH value at diagnosis ranged from 160-6,100 IU/liter (IU/L). Of the 23 patients, 9 had presenting LDH values greater than 500 IU/L and 8 of these patients relapsed or died; one child whose initial LDH was 600 IU/L remained alive and was in continuous remission 22 mo after diagnosis. Among 14 patients with presenting LDH values less than 500 IU/L, a single relapse occurred in one child 24 mo after diagnosis. He remained alive and in remission on therapy 44 mo after diagnosis. The other 13 children were in continuous first remission from 3-45 mo after diagnosis. In the total patient group, a strong association between presenting LDH values greater than 500 IU/L and eventual relapse and death (P less than 0.01) was observed. Results indicated that serum LDH is a reliable indicator of current disease status for patients with non-Hodgkin lymphoma and a useful confirmation of remission status; it cannot be used to predict impending return of disease. (10 Refs)

23. MALIGNANT TUMORS OF THE HEAD AND NECK AND BIOCHEMICAL MARKERS.

Doi Y, Takeuchi T, Hotate T, Kataura A, Nishio M, Sakurai T, Kamata N, Uchida M

Dept. Otolaryngology and Oral Surgery, Tonan Hosp., Sapporo, Japan

Gan No Rinsho; 27(11):1309-1317 1981

Concentrations of beta-aminoisobutyric acid (bAIBA) and beta-alanine (bA) were measured in the urine of 117 patients with malignant tumors of the head and neck and were compared to those in 158 patients with benign diseases of the head and neck who were thought to have high urinary concentrations of bAIBA and bA. Overall, 82/117 patients with malignant tumors had high concentrations of urinary bAIBA and 19/117 had high concentrations of urinary bA; 87/117 had high concentrations of either bAIBA or bA. Overall, 15/158 patients with benign diseases had high concentrations of bAIBA and 6/158 had high concentrations of bA; 18/158 had high concentrations of either bAIBA or bA. Histologically, high concentrations of bAIBA were observed in 66/82 patients with squamous cell carcinoma, and either bAIBA or bA concentrations were high in 68/82 patients with squamous cell carcinoma and 8/10 with malignant lymphoma. Compared to patients with squamous cell carcinoma, a higher percentage of the patients with malignant lymphoma had high concentrations of bA. bAIBA and bA were thought to have applications in the diagnosis of malignant tumors. (23 Refs) (In JPN)

24. THE RELATIONSHIP BETWEEN LYMPHOCYTE NUCLEAR MORPHOLOGY AND CELL CYCLE STAGE IN LYMPHOID NEOPLASIA.

Diamond LW, Weisenburger DD, Rappaport H
Dept. Pathology, Temple Univ. Sch. Medicine, Philadelphia, PA, 19140
Am J Hematol; 11(2):165-173 1981

A significant percentage of lymphoid cells isolated from three lymphoid neoplasms (nodular lymphoma mixed cell type, mycosis fungoides, and Sezary syndrome) had tetraploid or near-tetraploid DNA content, as determined by flow cytometric analysis. In each case, a morphologically distinct population of cells with large, irregular nuclei was present, the percentage of which corresponded to the percentage of tetraploid cells. In a fourth case (diffuse 'histiocytic' lymphoma), cells were sorted on the basis of DNA content from the G0-G1 compartment and compared morphologically to cells sorted from the S-G2 (M) compartment. The G0-G1 cells had clumped nuclear chromatin, lacked prominent nucleoli, and had a mean nuclear diameter of 10.18 +-1.22 um. The sorted cells with S-G2(M) DNA content had one to several prominent nucleoli and less clumped nuclear chromatin, and they were significantly larger, with a mean nuclear diameter of 13.76 +-1.59 um (p less than 0.00001). These preliminary results suggest that, in lymphoid malignancies, certain morphologic characteristics of individual lymphoid cells are related to their DNA content (level of ploidy) and/or the stage of the cell within its division cycle. (Author abstract) (18 Refs)

25. NATIONAL CANCER INSTITUTE RETROSPECTIVE STUDY OF THE NON-HODGKIN'S LYMPHOMAS: ABSTRACT (REPORT NO 7).

Henry K
(c/o G. Hudson) Dept. Oncology, Middlesex Hosp., London, W1, England
Clin Radiol; 32(5):499-500 1981

A retrospective study of the non-Hodgkin's lymphomas has been set up in order to assess and compare the five new classifications with that of Rappaport and to relate them to clinical data in terms of prognosis. Following analyses of the computer data, agreement has been achieved on an acceptable 'formulation' for use in clinical trials for classification of the non-Hodgkin's lymphomas which should prove valuable in allowing cross reference between different centers. (Author abstract) (1 Ref)

MALIGNANT LYMPHOMA: CLINICAL IMMUNOLOGY AND IMMUNOTHERAPY

26. RECEPTORS FOR HELIX POMATIA AGGLUTININ ON NORMAL AND NEOPLASTIC LYMPHOCYTES. A HISTOCHEMICAL STUDY USING PARAFFIN EMBEDDED TISSUE SECTIONS.

Tsutsumi Y
Dept. Pathology, Tokai Univ., Sch. Medicine, Boseidai, Isehara-city, Kangawa 259-11, Japan
Acta Pathol Jpn; 31(4):641-661 1981

In order to investigate the distribution and significance of receptors for Helix pomatia agglutinin (HPA), paraffin sections from several reactive and 71 neoplastic lymphoid tissues were utilized for a histochemical study after neuraminidase treatment. Lymphocytes in the germinal center and thymic cortex were mostly negative for the receptors, while most of the lymphocytes in the thymus-dependent area, some of those in the primary follicle or in the marginal zone and most of the plasma cells in the med ulla possessed the receptors on their surfaces. Nodular lymphomas, thymomas and diffuse lymphoblastic lymphomas were mostly negative in contrast to the positive reaction in diffuse poorly differentiated lymphomas of B-cell type and plasmocytomas. Diffuse histiocytic lymphomas and diffuse mixed lymphocytic and histiocytic lymphomas occasionally possessed the receptors, irrespective of their immunological markers. Hodgkin's cells were negative on their surfaces, but were occasionally positive in their cytoplasms as seen in case of histiocytes. From these results, HPA receptors could be neither T-cell nor B-cell differentiation marker. The possibility that HPA-receptor-negative lymphocytes may have a quick turn-over rate or a short life span is also discussed. (Author abstract) (30 Refs)

27. FOLLOW-UP OBSERVATIONS ON THE EFFECT OF HUMAN LEUKOCYTE INTERFERON IN NON-HODGKIN'S LYMPHOMA.

Louie AC, Gallagher JG, Sikora K, Levy R, Rosenberg SA, Merigan TC
Div. Oncology, Dept. Medicine, Stanford Univ. Sch. Medicine, Stanford, CA, 94305
Blood; 58(4):712-718 1981

Follow-up data for 11 patients with non-Hodgkin's lymphoma treated with partially purified human leukocyte interferon is presented. The interferon preparation used was 0.1% pure and treatment consisted of 5 x 10(6) U given im twice daily for 60 injections. One complete, three partial, and three minimal responses were observed in five of seven evaluable patients with nodular non-Hodgkin's lymphoma. Duration of response appears to be from 6 to 12 mo. One patient achieved a second partial response on retreatment with interferon in spite of having received chemotherapy in the interval between interferon treatments. No responses were seen in three patients with rapidly progressive diffuse histiocytic lymphoma. Dose-limiting toxicity is leukopenia, which necessitated modification or cessation of treatment in three patients. Nonhematologic toxicities consisted of fever, malaise, arthralgia, and loss of appetite. In conclusion, interferon has activity against non-Hodgkin's lymphoma, and prior treatment with chemotherapy does not preclude a response to interferon. (Author abstract) (13 Refs)

MALIGNANT LYMPHOMA: CHEMOTHERAPY

28. CHILDHOOD NON-HODGKIN'S LYMPHOMA: LONG-TERM RESULTS OF AN INTENSIVE CHEMOTHERAPY REGIMEN.

Gasparini M, Lombardi F, Bellani FF, Gianni C, Pilotti S, Rilke F
Istituto Nazionale Tumori, Via Venezian, 1 20133 Milan, Italy
Cancer; 48(7):1508-1512 1981

Twenty-nine consecutive children with untreated non-Hodgkin's malignant lymphoma were admitted to Istituto Nazionale Tumori of Milan during the period from 1974 through 1976 and underwent treatment with chemotherapeutic regimens consisting of Adriamycin, Cytoxan, vincristine, and prednisone (2 mo induction phase) and 6-mercaptopurine, methotrexate, Adriamycin, vincristine and prednison e (maintenance phase).

Each patient, regardless of clinical stage or histologic subgroup, was given the same chemotherapy. The complete response rate was 66%. Due to the high incidence of recurrence of the initial bulky lymphomatous mass and of spread to the central nervous system (CNS), local radiotherapy was given to 10 children and CNS prophylaxis (brain radiotherapy + intrathecal methotrexate) to 11 children. After a follow-up period in excess of 40 mo, there were five disease-free survivors (17%). Each patient who had a relapse died from the disease. The main reason for first treatment failure was relapse at the level of the primary bulklky tumor site or spread to the CNS. This type of CNS prophylaxis did not prevent relapse at this site. (Author abstract) (16 Refs)

29. CHEMOTHERAPY IN THE MANAGEMENT OF STAGE III/IV GRADE 1 NON-HODGKIN'S LYMPHOMAS (REPORT NO 17).

Hayhoe FG
(c/o Hudson) Dept. Oncology, Middlesex Hosp., London, W1, England
Clin Radiol; 32(5):547-552 1981

This report describes two comparisons of combination chemotherapy with cyclophosphamide, vincristine and prednisone (COP) with chlorambucil in the management of Stages III, IV Grade 1 non-Hodgkin's lymphoma. The first prospective randomized study was carried out by the BNLI between 1974 and 1976. In 1976, initial analyses of 90 assessable patients indicated that COP was more effective than chlorambucil but it was considered by the BNLI collaborators that chlorambucil should not be discarded because it was so much more acceptable to both patients and doctors. Long-term follow-up of this early trial indicated that the decision not to give up chlorambucil was justified. Examination of the results in 1980, which included 130 assessable cases, showed identical recurrence-free survival rates in the two groups. In the second study starting in 1977, the initial comparison was between chlorambucil and COP, but if progressive improvement was not achieved by 3 mo the patient was regarded as a nonresponder and switched to the other arm. Patients were also drawn for maintenance (with chlorambucil) or not at the time for entry into the trial. Analyses of the first 180 patients shows similar complete remission rates, actuarial survival rates and recurrence-free survival rates. There seems no advantage in using COP as first-line treatment rather than single agent chlorambucil, provided that non-responders are treated subsequently with combination chemotherapy. (Author abstract) (5 Refs)

30. EFFECT OF HIGH-DOSE THYMIDINE INFUSIONS IN PATIENTS WITH MYCOSIS FUNGOIDES.

Kufe DW, Wick MM, Moschella S, Major P
Div. Pharmacology and Medical Oncology, Sidney Farber Cancer Inst., 44 Binney St., Boston, MA
Cancer; 48(7):1513-1516 1981

The antitumor effect of thymidine has been demonstrated in patients with leukemi a and lymphoma. This report summarizes the treatment of three patients with mycosis fungoides, a chronic T-cell lymphoma. Four courses of thymidine (75 g/m2/day) were administered by continuous infusion for 4-7 days. Steady-state serum thymidine levels were in the range of 1-3 mM. Associated toxicities were minimal and consisted of mild headache and anorexia. Myelosuppression was manifested by transient declines in the peripheral WBC count. One patient had extensive clearing of diffuse erythematous plaques on the trunk and extremities that persisted for over 1 mo. A second patient had partial clearing of plaques that persisted for 2 wk following therapy and a third patient had a minimal response with 25% reduction in lymphadenopathy and noduloulcerative lesions. These responses indicate the effectiveness of thymidine as a single agent in the treatment of mycosis fungoides. (Author abstract) (17 Refs)

31. TREATMENT OF PARAPSORIASIS EN PLAQUES AND MYCOSIS FUNGOIDES WITH AN ORAL AROMATIC RETINOID (RO 10-9359).

Souteyrand P, Thivolet J, Fulton R
Clinique Dermatologique, Hopital E. Herriot, F-69374 Lyon Cedex 2, France
Retinoids: Advances in Basic Research and Therapy, Proceedings of the International Dermatology Symposium held in Berlin, W. Germany, 13-15 October, 1980. Orfanos CE, Braun-Falco O, Farber EM, Grupper C, Polano MK, and Schuppli R, ed. Berlin, Springer-Verlag, 527 pp., 1981.

The aromatic retinoid Ro 10-9359 (AR) was tested in 10 patients, including 3 with parapsoriasis en plaque (PPP), 6 with mycosis fungoides (MF), and 1 with Sezary's syndrome (SS). Three PPP and two MF patients received AR (1 mg/kg body wt/day for 1 mo and 0.7 mg/kg body wt/day thereafter) as sole treatment. Four MF and the 1 SS patient received AR (1 mg/kg body wt/day for the duration of treatment) in combination with psoralen-UV-A (PUVA) treatment. Among those receiving only AR two PPP patients showed clinical improvement; MF did not respond to AR treatment. Four MF patients who had had relapses after PUVA therapy showed complete clearing of lesions with combined AR and PUVA therapy. The SS patient showed improvement only on the palmo-plantar keratodermia. The mechanism by which AR produced results was not determined. (no Refs)

MALIGNANT LYMPHOMA: RADIOTHERAPY

32. RADIOTHERAPY IN THE TREATMENT OF LOCALISED NON-HODGKIN'S LYMPHOMA (REPORT NO 16).

Phillips DL
(c/o G. Hudson) Dept. Oncology, Middlesex Hosp., London W1, England
Clin Radiol; 32(5):543-546 1981

This report describes the experience of the BNLI in the treatment of localized (Stages I, II) non-Hodgkin's lymphoma (NHL). About a third of all patients with NHL presenting to collaborators in the BNLI were considered after investigation to have localized disease. This relatively large number suggests that some cases may have been understaged. Patients with Grade 1 disease were treated with either local irradiation or with local irradiation followed by chlorambucil. Survival rates in the two groups were essentially similar and it appeared that radiotherapy alone provided equally effective treatment. Patients with Grade 2 lymphomas were treated either with local irradiation or with local irradiation followed by COP. Primary nodal disease was not obviously affected by the addition of chemotherapy. Extranodal disease arising in the gut below the diaphragm appeared to be adversely affected by the irradiation which was of necessity spread over several wk, delaying the use of chemotherapy. Extranodal disease arising in the head and neck region is controlled in about 80% of patiens and the routine use of prophylactic combination chemotherapy confers no benefit to the patient. (Author abstract) (5 Refs)

33. TREATMENT OF MALIGNANT LYMPHOMAS OF THE OROPHARYNX.

Duhmke E, Schwarze EW
Radiologische Universitatsklinik, Arnold-Heller-Strasse 9, D-2300 Kiel, W. Germany
HNO; 29(9):302-307 1981

The natural history of malignant lymphomas of the oropharynx and their response to treatment are described by evaluating the courses of 41 patients, who after histological verification underwent radiotherapy in the Radiological Clinic of Kiel University between 1965 and 1979. The analysis of the malignant non-Hodgkin lymphomas according to the 'Kiel classification' reveals a clear predominance of the germinal center tumors and the high grade malignancies. The long-term results of treatment show a good prognosis for clinical stages I-II1 (2 adjacent lymph node or extranodal regions involved above the diaphragm, 'Ann Arbor'-classification modified by Musshoff) with a 85% probability of both survival and freedom of disease. For clinical stages II2-IV long-term actuarial survival and disease free survival were lowered to 51% and 23%. Whereas in 93% a complete tumor regression could be achieved by the primary treatment, one third of these patients developed a recurrence of the disease, mainly caused by incomplete therapy, such as missing the 'extended field' radiotherapy or a necessary chemotherapy because of old age, myelodepression or simply refusal of further treatment. According to the results of this study chemotherapy seems to be necessary from clinical stage II2 on (2 distant lymph node or extranodal regions or three or more regions located anywhere involved above the diaphragm). Finally a refined locoregional irradiation technique for malignant lymphomas of the oropharynx is described: fast electrons and cobalt rays in daily alteration for the posterior cervical lymph nodes. Last but not least, we present the unusual treatment schemes of the 'Kiel Lymphoma Study Group' for malignant non-Hodgkin-Lymphomas of different histologies and stages. (Author abstract) (9 Refs) (In GER)

34. RESULTS OF RADIOTHERAPY OF RETICULOSARCOMA LOCALIZED IN THE HEAD AND NECK REGION ACCORDING TO INITIAL SITE (MEETING ABSTRACT).

Kita M, Tazaki E, Ono I, Ebihara S, Kitagawa T, Takeda C, Umegaki Y
Dept. Radiology, Tokyo Women's Medical Sch., Shinjuku-ku, Tokyo 162, Japan
Program and Preprints of the 5th Annual Congress of Japan Society of Head and Neck Tumor held in Osaka, Japan, 29-30 May, 1981. Japan Society of Head and Neck Tumor, Chiba 280, Japan, 109 pp., 1981.

Between 1969 and 1978, 149 patients with malignant lymphomas that were localized in the head and neck region and were at Stages I and II (no lesions in the infraclavicular region) were seen at the National Cancer Center. Of these patients, 117 had reticulosarcoma, and 96 of those whose initial site was the lymph nodes were analyzed for the effect of the radiotherapy they had been given. The initial site was Waldeyer's ring in 25, cervical lymph nodes in 9 and both in 62 patients. Mainly radiotherapy was given, and in 15 it was combined with chemotherapy. The field of irradiation was mainly the primary lesion and the neighboring lymph node region. The dose directed at the lesion most often totaled 4,000-5,000 rad. Clinically 80% of the tumors disappeared when the total dose was less than 4,500 rad. The postradiotherapy recurrence rate was 48.9%, and 81% of the relapses occurred within 1 yr after radiotherapy. The site of the first relapse was the superficial lymph nodes in 55.6% and the abdomen in 31.5% of these patients. Of these recurrences, 13% occurred within the field of irradiation, and they occurred in the cervical lymph nodes in all except two patients who had relapse. Nine of the patients who had relapse had been given a total of less than 4,500 rad, and one had been given 5,000 rad or more. Relapse occurred during radiotherapy in two patients. The 6-mo, 1-yr, 2-yr and 5-yr survival rates for the patients whose initial site was Waldeyer's ring were 100%, 95.8% 87.5% and 82.6%, respectively, those for the patients whose initial site was the cervical lymph nodes were 71.4%, 57.1%, 28.6% and 28.6%, respectively, and those for the patients whose initial site was both were 84.2%, 57.9%, 42.1% and 38.9%, respectively. (no Refs) (In JPN)

MALIGNANT LYMPHOMA: MULTIMODAL THERAPY

35. NON-HODGKIN'S LYMPHOMA OF WALDEYER'S RING (MEETING ABSTRACT).

Masaki N, Ikeda H, Shigematsu Y, Aosasa K
Dept. Radiology, Medical Sch., Osaka Univ., Kita-ku, Osaka 530, Japan
Program and Preprints of the 5th Annual Congress of Japan Society of Head and Neck Tumor held in Osaka, Japan, 29-30 May, 1981. Japan Society of Head and Neck Tumor, Chiba 280, Japan, 109 pp., 1981.

Of 331 patients who had Stage I or Stage II non-Hodgkin's lymphoma and had radiotherapy between 1961 and 1979, 202 had tumors in Waldeyer's ring (44 Stage I, 158 Stage II). The 5-yr survival rate for the patients with Stage I and Stage II non-Hodgkin's lymphoma of Waldeyer's ring was 74.4% and 40.6%, respectively. The results of therapy in the patients seen since 1971 was about 20% better than those in the patients seen before then; the 5-yr survival rate for the patients with Stage I and Stage II cancer seen since 1971 was 86.4% and 54.7%, respectively. For the patients with stage II cancer who had been seen since 1971 and given chemotherapy to introduce remission, the 5-yr survival rate was 76%, while for the patients given only radiotherapy it was 49%. Relapse was seen in 30% and 60% of the patients with Stage I and Stage II cancer, respectively. Relapse occurred within 1 yr after radiation therapy in about 80%, and within 2 yr in 90% of the patients. However, relapse occurred after 3 yr in six patients, one patient having a relapse after 7 yr and 11 mo. The distant lymph nodes were the most frequent site of relapse, followed by the stomach and upper abdominal lymph nodes. (no Refs) (In JPN)

MALIGNANT LYMPHOMA: SUPPORTIVE CARE

36. LITHIUM CARBONATE TREATMENT IN PREVENTING GRANULOCYTOPENIA INDUCED BY ANTIBLASTIC THERAPY.

Orlando S, Baroni MC, Crotti G, Mineo F, Capra A, Coiro V, Delsignore R
Istituto di Clinica Medica Generale e Terapia Medica, Universita degli Studi di Parma, Parma, Italy
G Clin Med; 62(5):351-359 1981

Thirteen polychemotherapy-treated patients (9 men, 4 women; 17-73 yr old) were diagnosed as having non-Hodgkin's lymphoma (7); 2 Hodgkin's lymphoma (2); acute non-lymphoblastic leukemia (2); and multiple myeloma (2). During this study, the patients were administered one to four cycles of polychemotherapy, using the same dosages as before, together with Li carbonate (10 mg/kg/day). Comparing the results with those obtained previously when no Li carbonate was given, counts of WBC and neutrophilic granulocytes were significantly higher. With the addition of the Li carbonate, it was possible to complete as scheduled the dosage, time intervals, and cycles of chemotherapy. Although this combination treatment did not eliminate infections, their time spans were shorter, and they could be controlled more easily. Even after 7 mo of the therapy, the Li carbonate effect was quantitatively and qualitatively the same. No side-effects due to the Li carbonate were observed. The mode of action of Li carbonate was discussed. (25 Refs) (In ITA)

MALIGNANT LYMPHOMA: CASE REPORTS

37. COMBINED GATED CARDIAC BLOOD POOL SCINTIGRAPHY AND 67GA-CITRATE SCINTIGRAPHY FOR DETECTION OF CARDIAC LYMPHOPROLIFERATIVE DISORDERS.

Winzelberg GG, Rapoport F, Boucher CA, Carey RW, Mckusick KA, Strauss HW
Div. Nuclear Medicine, Shadyside Hosp., 5230 Centre Ave., Pittsburgh, PA, 15232
Radiology; 141(1):191-192 1981

Two cases are reported in which combined radionuclide imaging using gated cardiac blood pool scintigraphy and 67Ga-citrate scintigraphy aided in evaluating lymphomatous involvement of the heart and distinguishing tumor involvement from other cardiac disorders. (Author abstract) (5 Refs)

MALIGNANT LYMPHOMA: SELECTED REPORTS ON ETIOLOGY AND EPIDEMIOLOGY

38. DIVERSE FAMILIAL MALIGNANT TUMORS AND EPSTEIN-BARR VIRUS.

Purtilo DT, Liao SA, Sakamoto K, Snyder LM, DeFlorio D, Bhawan J, Paquin L, Yang JP, Hutt-Fletcher LM, Muralidharan K, Raffa P, Saemundsen AK, Klein G
Dept. Pathology, Univ. Nebraska Medical Center, 42nd and Dewey Ave., Omaha, NE, 68105
Cancer Res; 41(11,part1):4248-4252 1981

Continued monitoring of a family for new malignant tumors has revealed diverse immunological and neoplastic disorders during a 15-yr period. In 1966, the proband developed lymphoma. In 1975, his antibody titers to Epstein-Barr virus (EBV) became elevated, and again, he developed a malignant lymphoma. He also had borderline hypo-Ig A, died of glioblastoma multiforme in 1977, and at autopsy, had adenomatous colonic polyps. His eldest brother has normal Ig levels, but developed immune thrombocytopenia in 1973 and had elevated EBV antibody titers in 1980. Another brother had hypo-Ig A, thymoma in 1965, and adenomas and adenocarcinoma of the colon. Two other brothers succumbed to glioblastoma in 1968 and 1969. The father of the proband had bronchiectasis in 1952, hypo-Ig M documented in 1972, and elevated EBV antibody titers 5 yr preceding development of a malignant lymphoma. The latter contained 10 EBV genome equivalents/cell by EBV viral DNA/DNA reassociation kinetics analysis. The proband's grandmother had died of an Ig G-secreting myeloma in 1977, and his grandfather had borderline low Ig M, elevated EBV antibody titers, and hypopharyngeal carcinoma in 1980. Predisposition to oncogenesis in this family was probably inherited. (Author abstract) (26 Refs)

39. LYMPHOMA IN THREE MEMBERS OF THE SAME FAMILY.

Spremolla G, Petrini M, Ambrogi F, Grassi B
Via di Padule, 16, 56100 Pisa, Italy
Haematologica (Pavia); 66(2):228-232 1981

Cases of three women from the same family with lymphoma, two well-differentiated lymphocytic and one Hodgkin's disease, are described. One 68-yr-old woman presented with generalized adenopathy, epigastric pain, and postprandial vomiting. Supraclavicular biopsy allowed the diagnosis of well-differentiated lymphocytic lymphoma. The patient was treated with polychemotherapy. A sister of Patient 1 had been diagnosed at the age of 41 yr as having Hodgkin's disease. Following alternate phases of remission and deterioration, and after treatment with numerous polychemotherapeutic cycles, the patient had been asymptomatic for 5 yr. A 39-yr-old niece of Patients 1 and 2 presented with multiple laterocervical and supraclavicular adenopathies. Supraclavicular lymph node biopsy revealed well-differentiated lymphocytic lymphoma. She was treated with a polychemotherapy regimen and remained asymptomatic. The etiology of lymphoma is discussed with respect to these three cases of lymphoma found in one family; notable aspects are the simultaneous presence of two very different types of lymphoma and concordance in the female sex. Genetic factors seem more important than infectious causes. (19 Refs)

MALIGNANT LYMPHOMA: SELECTED PRE-CLINICAL STUDIES

40. INDUCTION OF LYMPHOSARCOMA IN SHEEP BY BOVINE LEUKEMIA VIRUS.

Kenyon SJ, Ferrer JF, McFeely RA, Graves DC
(c/o Ferrer) Sch. Veterinary Medicine, Univ. Pennsylvania, New Bolton Center, Kennett Square, PA, 19348
JNCI; 67(5):1157-1163 1981

Newborn sheep inoculated with phytohemagglutinin (PHA)-treated short-term cultures of lymphocytes from cattle infected with bovine leukemia virus (BLV) or with a BLV-infected long-term culture of bovine leukemic lymphocytes became persistently infected with BLV. Fifty percent or more of the sheep died with histologically confirmed lymphosarcomas. Cytogenetic studies of representative cases demonstrated that the tumors did not result from the progressive growth of neoplastic lymphocytes in the inoculum but rather from the neoplastic transformation of the recipient's lymphoid cells. Neither BLV infection nor lymphosarcoma was observed in control uninoculated sheep or in sheep given injections of PHA-treated cultures of lymphocytes from BLV-free cows. The virus recovered from the tumorous sheep was indistinguishable from BLV morphologically, antigenically, and biologically, and its reverse transcriptase had the same cation preference and immunologic properties as the BLV enzyme. Persistent BLV infection and lymphosarcoma were also observed in a group of sheep inoculated neonatally with BLV-containing cell-free culture supernatants. These results extend previous observations on the high susceptibility of sheep to BLV infection and provide definitive evidence that BLV is a tumor-inducing virus. (Author abstract) (33 Refs)

41. IMMUNOPATHOLOGY OF NATURAL AND EXPERIMENTAL LYMPHOMAS INDUCED BY WILD MOUSE LEUKEMIA VIRUS.

Bryant ML, Scott JL, Pal BK, Estes JD, Gardner MB
(c/o Gardner) Dept. Pathology, Univ. California Sch. Medicine, Davis, CA, 95616
Am J Pathol; 104(3):272-282 1981

Naturally occurring lymphomas of Lake Casitas (LC) wild mice, and the lymphomas induced by LC murine leukemia virus (MuLV) in Swiss mice from the National Institutes of Health, displayed remarkably similar gross, microscopic, and functional characteristics. They spared the thymus, arose primarily in the splenic red pulp, became leukemic, and were comprised of stem cells lacking classic T- and B-cell markers. Cytoplasmic and surface Ig were undetectable in 34 of 35 spontaneous LC lymphomas and in any of 10 LC MuLV-induced lymphomas in NIH Swiss mice. Assays for Ig secretion, complement (C'3) and Fc receptors, T hy 1.1,2 antigens, Ly 1,2 antigens, and erythroid and myeloid markers were negative on all of the spontaneous and experimental lymphomas. Cell lines were derived from five spontaneous lymphomas of LC mice. Three lines were characterized as null cells, one line as B cells, and one line as macrophages. All cell lines were diploid. The wild mouse spontaneous lymphomas, and lymphomas experimentally induced by LC MuLV in laboratory mice, provide a useful model for childhood acute lymphoblastic leukemia and for study of the early steps of B-lymphocyte differentiation. (Author abstract) (64 Refs)

42. ENHANCED LYMPHOMA INCIDENCE IN BALB/C MICE AFTER ULTRAVIOLET LIGHT TREATMENT.

Ebbesen P

Inst. Cancer Res., Radiumstationen, Norrebrogade 44, DK-8000 Aarhus C., Denmark

JNCI; 67(5):1077-1078 1981

Following UV irradiation of BALB/c mice 3x a wk for 9 mo, lymphatic leukemia or reticulosarcoma developed in 44 (12%) of 378 mice whose backs were shaved and whose ears were intact. Only 11 (5%) of 224 UV-irradiated mice whose backs were shaved and whose ears were removed developed lymphomas. Among 311 unirradiated mice whose backs were shaved, 9 lymphomas (3%) occurred. The diagnosis of leukemia or reticulosarcoma was confirmed by microscopy and transplantation. Among irradiated mice, ear tumors developed in 24% of the mice with intact ears, whereas skin tumors developed on the shaved backs in 4% of the mice whose ears were removed and also in 4% of the mice with intact ears. (Author abstract) (6 Refs)

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HODGKIN'S DISEASE: DIAGNOSIS AND STAGING

1. USE OF CYTOCHEMICAL STUDIES FOR EVALUATION OF HODGKIN'S DISEASE ACTIVITY IN CHILDREN.

Vialushkina MD, Vialushkin BIa
Res. Inst. Pediatrics, Moscow, USSR
Lab Delo; (9):517-520 1981

The enzymatic activity of peripheral blood lymphocytes, neutrophils, and platelets was studied in 33 children (4-14 yr old) with Hodgkin's disease. Six children had Stage IIA, 7 had Stage IIIA, 15 had Stage IIIB, and 5 had Stage IVB. Elevated activity of neutrophil alkaline phosphatase with corresponding increased activity of succinate dehydrogenase and alpha-glucosephosphate dehydrogenase in the lymphocytes and neutrophils were recorded in the patients with Stages IIIB and IVB. (11 Refs) (In RUS)

HODGKIN'S DISEASE: CLINICAL IMMUNOLOGY AND IMMUNOTHERAPY

2. IMMUNODEFICIENCIES IN HODGKIN'S DISEASE. PART I: T CELL-MEDIATED IMMUNITY.

Gupta S
Clinical Immunology Service, Sloan-Kettering Inst., New York, NY
Clin Bull; 11(2):58-65 1981

The association between Hodgkin's disease and immunodeficiency states is reviewed. Immunodeficiencies may predispose patients with Hodgkin's disease to a second neoplasm and to increased risk of infectious complications, especially viral and fungal (eg herpes zoster and cryptococcosis). Both in vivo and in vitro T cell-mediated immune responses in patients with various stages of Hodgkin's disease are discussed, including delayed type hypersensitivity, homograft rejection, lymphocyte response to soluble antigens and to mitogens and allo-antigens, analysis of T cells and T cell subsets, and cytotoxic response and mechanisms responsible for T cell-mediated immunodeficiencies. The role played by splenectomy in treatment of Hodgkin's disease is discussed. (71 Refs)

3. LONGITUDINAL STUDIES OF BLOOD LYMPHOCYTE CAPACITY IN HODGKIN'S DISEASE.

Bjorkholm M, Wedelin C, Holm G, Johansson B, Mellstedt H
Dept. Medicine, Danderyd's Hosp., S-182 88 Danderyd, Sweden
Cancer; 48(9):2010-2015 1981

Blood lymphocyte functional capacity and serum Ig were studied in 40 patients with Hodgkin's disease (HD) admitted to Radiumhemmet, Stockholm, before treatment and in complete remission 2-56 mo following termination of radiotherapy (total nodal irradiation [TNI]; n = 29) or chemotherapy (MOPP; n = 11). Lymphocyte studies included determination of total lymphocyte and T-cell counts and evaluation of spontaneous DNA synthesis during the first day of culture and mitogen-(concanavalin A, pokeweed mitogen) and antigen (purified protein derivative, PPD)-induced activation on the 3rd day. Blood lymphocyte and T-cell counts decreased dramatically following TNI. A slow restitution was seen, but pretreatment levels were not reached even 4 yr following therapy. The responses to ConA and PPD but not PWM were significantly reduced shortly after TNI. The mitogen response did not increase with time as did the PPD response. Lymphocyte counts and lymphocyte stimulation, which were severely depressed before treatment of patients in the chemotherapy group, remained unchanged 2-36 mo after termination of therapy. A significant reduction of IgM levels was observed regardless of the mode of treatment. Splenectomy prevented the profound reduction of blood lymphocyte and T-cell counts following therapy but did not influence the other immunologic variables under study. (Author abstract) (43 Refs)

HODGKIN'S DISEASE: SELECTED PRE-CLINICAL STUDIES

4. LYMPHOPROLIFERATION AND HETEROTRANSPLANTATION IN NUDE MICE: TUMOR CELLS IN HODGKIN'S DISEASE.

Diehl V, Kirchner HH, Schaadt M, Fonatsch C, Stein H
Department fur Innere Medizin, Medizinische Hochschule, Karl-Wiechert- Allee 9, 3000 Hannover-Kleefeld, W. Germany
Haematol Blood Transfus; 26:229-234 1981

Histologically proven Hodgkin's disease (HD) derived material was used to establish four long term cultures. These in vitro cells had morphologic, cytochemical and cytogenetic features of their in vivo ancestors. Two of these cultures were obtained from pleural effusions of HD nodular sclerosing type, Stage IV B (diagnosed, one in 1972 and another in 1976). They shared these same features: non-B-T lymphocytes, non-macrophages, non myeloid cells, Epstein-Barr virus genome negative, monoclonality, multiple numerical and structural chromosome aberrations, and tumor formation after intracranial xenotransplantation in nude mice. After sc inoculation both lines failed to induce tumors. When one of them was embedded in a fibrin clot prior to transplantation, infiltrative tumor growth resulted after sc inoculation. Morphology of the two cell lines was very similar to Hodgkin (H) and Sternberg-Reed (SR) cells. Biological and immunological characterization of the two lines showed identical pattern observed in freshly prepared H and SR cells. They resemble very closely cultured H cells described by Kaplan. (14 Refs)

HODGKIN'S DISEASE: REVIEWS

5. ON THE BIOLOGY AND IMMUNOLOGY OF HODGKIN'S DISEASE.

Kaplan HS
Dept. Radiology, Cancer Biology Res. Lab., Stanford Univ. Medical Sch., Stanford, CA, 94305
Haematol Blood Transfus; 26:11-23 1981

Biological and immunological characteristics of Hodgkin's diseases (HD) are presented. Giant cells of HD satisfy two of the most fundamental attributes of neoplasia: aneuploidy and clonal derivation. Cell culture and immunofluorescence studies have provided information concerning the origin and nature of the HD giant cells. Their capacity for sustained proliferation in vitro, aneuploidy, and heterotransplantability establishes their neoplastic character, whereas the cell marker studies, phagocytic activity, positive staining reactions for nonspecific esterase, and capacity to excrete lysozyme strongly suggest that they are derived from the macrophage or other closely related cells of the mononuclear phagocyte system rather than from the lymphocyte. The natural history and mode of spread of HD is discussed. Study results indicating that virtually all HD patients, including those with localized involvement, suffer from a selective, often subtle, impairment of cell-mediated immunity are presented. In vivo, this deficit is expressed by an increased susceptibility to certain types of bacterial, fungal, and viral infections and by decreased capacity for delayed hypersensitivity reactions to recall antigens or chemical allergens. A spectrum of in vitro test results are also impaired. These alterations may be due to functional alterations of T-lymphocytes rather than to quantitative depletion of either T- or B-lymphocytes. Human inhibitors in the sera of HD patients and suppressor cell effects have also been implicated. (37 Refs)

MALIGNANT LYMPHOMA: DIAGNOSIS AND STAGING

6. PROGNOSTIC RELEVANCE OF THYMIDINE KINASE ISOZYMES IN ADULT NON-HODGKIN'S LYMPHOMA.

Ellims PH, Gan TE, Medley G, Van Der Weyden MB
(c/o Van Der Weyden) Dept. Medicine, Monash Univ., Alfred Hosp., Commercial Road, Prahran, 3181, Victoria, Australia
Blood; 58(5):926-930 1981

To determine whether thymidine kinase (TK) isozyme status adds clinically useful information in adult non-Hodgkin's lymphoma (NHL), we have analyzed peripheral blood plasma and lymphocytes of 44 patients with NHL for either TK1 or TK2 isozyme activity. On the basis of isozyme status, patients could be divided into two groups that did not differ significantly with respect to known determinants for survival. The median survival of patients exhibiting peripheral blood TK1 thymidine kinase activity was 40 wk and that of individuals with TK2 activity was in excess of 200 wk. These data suggest that peripheral blood TK1 isozyme is a useful independent biochemical marker for a subgroup of NHL who respond poorly to current therapy and thus require new therapeutic approaches. (Author abstract) (32 Refs)

7. SEVERAL MARKER ANALYSES OF T-LYMPHOMA CELLS IN EIGHT JAPANESE ADULTS.

Nasu K, Tatsumi E, Takiuchi Y, Kita K, Nishikori M, Shirakawa S, Uchino H
First Div. Internal Medicine, Faculty Medicine, Kyoto Univ., Sakyo-ku Kyoto 606, Japan
Am J Clin Pathol; 76(5):670-678 1981

Lymphoma cells in eight adult Japanese patients with no evidence of overt leukemia throughout their clinical course were demonstrated to be of T-cell nature by combining studies of various immunologic cell surface markers and cytochemistry. The histologic diagnosis of these patients was diffuse histiocytic lymphoma in four patients, poorly differentiated lymphocytic lymphoma in two patients and mixed histiocytic and lymphocytic lymphoma in two patients, according to Rappaport's classification. In seven of the eight patients, the malignant appearance and the large number of E-rosetting cells readily led to the diagnosis of T cell lymphoma. Human Ia-like antigens were unexpectedly detected on the malignant T cells in seven of the eight patients. TdT activity was elevated in two of the four patients tested. Acid phosphatase activity was always observed in the neoplastic T-cells, and this activity was tartrate resistant. Focal activity of acid alpha-naphthyl acetate esterase was detected in the malignant cells with somewhat mature appearances, but large immature cells had no or weak dispersed activity. Except for E-rosetting ability, malignant T-cells showed such variable properties that multiple marker analyses seem to be necessary in the diagnosis and the prediction of prognosis of these disorders. Frequent occurrence of T-cell malignancy in Japan was also discussed. (Author abstract) (52 Refs)

8. ENZYME POLYMORPHISM AS A BIOCHEMICAL CELL MARKER: APPLICATION TO THE CELLULAR ORIGIN AND HOMOGENEITY OF HUMAN MACROPHAGES AND TO THE CLASSIFICATION OF MALIGNANT LYMPHOMAS.

Radzun HJ, Parwaresch MR, Lennert K
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Haematol Blood Transfus; 26:222-224 1981

The polymorphism of lysosomal acid esterase in normal blood monocytes upon prolonged exposure of the monocytes to uncoated glass surfaces (as revealed by the isoelectric points of its major isoenzymes) gradually shifts from a blood monocyte pattern to the pattern characteristic of sessile peritoneal macrophages. The lysosomal acid phosphatase of B lymphocytes, which also has a characteristic isoenzyme isoelectric-point polymorphism, exhibits demonstrable alterations in its components in cases of chronic lymphocytic B-cell leukemia, follicular lymphoma, lymphoplasmacytic/lymphoplasmacytoid lymphoma, and plasmacytoma. These examples demonstrate that enzyme polymorphism may be useful as a biochemical marker for the characterization of maturational stages, functional derivatives, and neoplastic variants of a certain cell line. (7 Refs)

9. LYMPHOBLASTIC LYMPHOMA: A CLINICOPATHOLOGIC STUDY OF 95 PATIENTS.

Nathwani BN, Diamond LW, Winberg CD, Kim H, Bearman RM, Glick JH, Jones SE, Gams RA, Nissen NI, Rappaport H
City of Hope Natl. Medical Center, Duarte, CA, 91010
Cancer; 48(11):2347-2357 1981

A retrospective clinicopathologic study of lymphoblastic lymphoma was based on 95 patients from the files of the Repository Center for Lymphoma Clinical Studies. All patients were treated according to different protocols of Cooperative Oncology groups sponsored by the NCI. The patients ranged in age from 4 to 84 yr, with a median of 30 yr. Sixty-eight patients were male and 27 were female, with respective median ages of 27 and 50 yr. The male-to-female ratio was 2.5:1. Forty patients had mediastinal masses; 30 (75%) of whom were male. The median survival of all patients was 17 mo (range 1-100 mo). To ascertain the influence of various clinical and morphological parameters on survival, univariate and multivariate statistical analyses were performed. Patients older than 30 yr of age had significantly lower incidences of mediastinal involvement ($p = 0.01$), number of mitotic figures ($p = 0.04$), and development of leukemia ($p = 0.02$) than patients younger than 30. Whereas lymphoblastic lymphoma is generally considered to be a disease of children and young adults, this study indicates that lymphoblastic lymphoma occurs in all age groups. These findings further suggest that lymphoblastic lymphoma may have a different biologic behavior in older patients. (Author abstract) (29 Refs)

10. LYMPHOBLASTIC LYMPHOMA IN CHILDREN: THEIR RECOGNIZABILITY AS T- OR B-CELL NEOPLASMS IN HISTOLOGICAL SLIDES (ROUTINE SECTIONS).

Schwarze EW, Pileri S, Tolksdorf G, Kampert-Blumberg J
Institut fur Pathologie der Universitat, Hospitalstrasse 42, D-2300 Kiel, W. Germany
Klin Paediatr; 193(3):131-136 1981

A blind study was made of sections from tumor and lymph node biopsy material from patients with confirmed lymphoblastic lymphoma (lb L). Sixty patients included 51 children, one of whom had a virologically confirmed Burkitt's tumor. Routine serial sections were stained with hematoxylin-eosin and Giemsa stain, Gomori silver stain, or PAS-reaction. Of 20 cases diagnosed by immunologic, cytochemical, or virological analysis as T-, B-, or non-T/non-B lb L, 18 were correctly diagnosed by histological examination alone. Histological diagnosis matched definitive diagnosis in 48 of 51 children. T-cell lb L was characterized by equal complete and partial lymph node involvement, a high frequency of diffuse infiltration, few reticular fibers, and epithelioid venules in 50% of cases. B-cell lb L was characterized by 75% complete lymph node involvement, diffuse and nodular infiltration in 40% of cases, collagenous fibers in 55%, infiltrate necrosis in 65%, 'starry-sky' macrophages in 85%, and eosinophils in 30%. Intracellular structure and staining for acid phosphates also were of diagnostic significance. (36 Refs) (In GER)

11. SUBCATEGORIES OF HISTIOCYTIC LYMPHOMA: ASSOCIATIONS WITH SURVIVAL AND REPRODUCIBILITY OF CLASSIFICATION. THE SOUTHEASTERN CANCER STUDY GROUP EXPERIENCE.

Whitcomb CC, Cousar JB, Flint A, Crissman JD, Bartolucci AA, Durant JR, Gams RA, Collins RD, Byrne GE
(c/o Byrne) Dept. Pathology (D-33), Univ. Miami Sch. Medicine, Post Office Box 016960, Miami, FL, 33101
Cancer; 48(11):2464-2474 1981

Five pathologists reviewed histologic slides from 134 cases of histiocytic lymphoma and subclassified these cases using the Lukes-Collins classification system. Of 98 morphologically subclassifiable cases, 85 were distributed among three categories, each presumed to represent a lymphoma of follicular center cell origin. The remaining 12 cases were classified among three additional categories. The cases within the three follicular center cell categories, considered collectively, had a significantly better survival than did the cases within the other three categories considered as a whole. The pathologists classified cases generally as being of a follicular center cell type with a high degree of reproducibility, but their individual classifications varied significantly with respect to more specific morphologic categories. Suboptimal quality of histologic sections was a significant factor contributing to problems in morphologic classification. Ancillary immunologic techniques may be required for definitive subclassification of large cell lymphomas. (Author abstract) (20 Refs)

12. LYMPHOCYTIC LYMPHOMA SIMULATING HAIRY CELL LEUKEMIA: A CONSIDERATION OF RELIABLE AND UNRELIABLE DIAGNOSTIC FEATURES.

Palutke M, Tabaczka P, Mirchandani I, Goldfarb S
Dept. Pathology, Wayne State Univ. Sch. Medicine, 540 East Canfield Ave., Detroit, MI, 48201
Cancer; 48(9):2047-2055 1981

Morphologic, immunologic and functional characteristics of an unusual poorly differentiated diffuse lymphocytic lymphoma closely resembling hairy cell leukemia are presented and the diagnostic features of the latter disease are reviewed. The malignant cells morphologically resembled hairy cells at the light as well as electron microscopic level. They had surface characteristics of both T and B lymphocytes, were phagocytic, and adhered to glass. The spleen was smooth and resembled that seen in hairy cell leukemia. Although there was a predilection for the red pulp of the spleen, there was a lack of characteristic pseudosinus formation, and areas of predominantly white pulp involvement considered characteristic of lymphocytic lymphoma were found after extensive examination. (Author abstract) (26 Refs)

13. MULTIPLE HISTOLOGIC SUBTYPES OF NON-HODGKIN'S LYMPHOMA: CLINICAL AND PATHOLOGIC FEATURES.

Leyser S, Variakojis D, Mintz U, Vardiman JW, Ultmann JE
(c/o Variakojis) Dept. Pathology, Univ. Chicago, 950 East 59th St., Chicago, IL, 60637
Cancer; 48(9):2063-2069 1981

Twenty patients with non-Hodgkin's lymphoma (NHL) had different histologic subtypes of NHL in multiple sites or in a single tumor mass either at the time of their initial biopsy and staging (13 patients) or in the course of their disease (7 patients). These 20 cases represent 3.7% of all patients with NHL seen at the University of Chicago between January 1968 and May 1979. The 5-yr actuarial survival rate for all 20 patients was 68%. For those 13 patients who had multiple histologic subtypes at the initial workup, the 5-yr survival rate was 45%; for the 7 patients who developed a new histologic subtype later in the course of the disease, the 5-yr survival rate was 85%. In the latter group of patients, however, the initial biopsy specimens demonstrated better prognostic subtypes, and the median survival from the time of diagnosis of a new, less favorable histologic subtype averaged only 4 mo. These findings indicate that the prognosis is related to the least favorable histologic subtype present, unless this is only a minor component of a composite lymphoma or is limited to one extranodal site. (Author abstract) (39 Refs)

14. VALUE OF ULTRASONIC TOMOGRAPHY FOR THE DIAGNOSIS OF LYMPHOMA. PART 2: COMPLEMENT OR ALTERNATIVE TO LYMPHOGRAPHY?.

Schuller M, Redlow H, Raab K, Luning M, Schilling H
Institut fur Rontgendiagnostik, Bereich Medizin der Humboldt-Universitat, Schumannstr. 20/21, DDR-1040 Berlin, E. Germany
Radiol Diagn (Berl); 22(3):328-334 1981

Five hundred patients with suspected retroperitoneal lymphoma were subjected to ultrasonography (US) and lymphography (LG). Concordant findings were obtained by the two methods in 424/500 cases (84.8%). The LG findings were correct negative in 347 cases, false negative in 5, correct positive in 106, false positive in 14, and uncertain in 28. The US findings were correct negative in 363 cases, false negative in 9, correct positive in 102, false positive in 8, and uncertain in 18. The accuracy was 90.6% for LG and 93% for US. LG was found more advantageous in the diagnosis of small lymph node metastases, but US helped detected lymph nodes not accumulating contrast medium. US should be employed for all tumors likely to metastasize intraabdominally. US can be used as an alternative to LG for such indications as contraindication to lymphography, follow-up after the elimination of the contrast medium and unsuccessful LG. (no Refs) (In GER)

15. WHOLE BODY GALLIUM SCANNING IN MALIGNANT LYMPHOMA - ITS ROLE IN 1980 (MEETING ABSTRACT).

McLaughlin AF, Chu J, Howman-Gills R
Department of Nuclear Medicine, Royal Prince Alfred Hospital, Camperdown, New South Wales, Australia
Aust NZ J Med; 11(4):436 1981

Whole body gallium scanning is not a new technique but recent improvements in instrumentation (triple pulse height analysis, improved resolution and area scanning with gamma cameras), have markedly improved its sensitivity. It is now used extensively in our institution for the assessment of lymphoma patients: (1) as an initial baseline study: (2) possible extra nodal disease: and (3) for recurrence disease. Whole body gallium studies were performed at 48 and 72 hr after injection. They were performed on a large field camera, using triple pulse height analysis and area scanning. Spot views of the head and neck, thorax, abdomen and pelvis were routine at the 72 hr study and other views were performed where appropriate. Grey Scale Ultrasound of the abdomen was performed in all cases. Eighty-three studies were performed on patients with Hodgkin's disease (HD) and 104 studies in patients with non-Hodgkin's lymphoma (NHL). Sixty-two patient studies with HD were deemed to be active clinically. Fifty-nine had positive gallium scans, giving a sensitivity of 95%. Twenty-one patient studies were in clinical remission, but three had positive scans giving a specificity of 76%. Eighty patient studies with NHL were deemed to be active clinically. Sixty-nine had positive gallium scans giving a sensitivity of 86%. Twenty-four patient studies were in clinical remission but three had positive scans giving a specificity of 88%. Whole body gallium studies using contemporary instrumentation are a highly sensitive test for the detection of active malignant lymphomatous disease. In our experience its sensitivity in NHL is higher than previously reported. It is an essential part of the work up of all patients with lymphoma. (no Refs)

16. PITFALLS IN THE DIAGNOSIS OF LYMPHOMA OR LEUKEMIA IN CEREBROSPINAL FLUID (MEETING ABSTRACT).

Borowitz MJ, Bigner SH, Johnston WW
Division of Cytopathology, Dept. of Pathology, Duke University Medical Center, Durham, NC
Acta Cytol (Baltimore); 25(4):438 1981

Cytopathologic distinction between reactive processes involving cerebrospinal fluid (CSF) and leukemia or lymphoma is frequently difficult. We reviewed membrane filters and all available cytocentrifuge preparations of 74 CSF specimens (from 46 patients) that was originally considered diagnostic of or suspicious for lymphoma or leukemia among a total of 3,000 CSF specimens examined during 1979. One-third of the reviewed specimens were in retrospect attributable to a specific nonmalignant etiology and could be grouped into three morphologic-etiologic categories: (1) viral or fungal infections, characterized by either small immature lymphocytes with nucleoli that were confused with chronic lymphocytic leukemia (a lesion that rarely involves CSF) or large 'histiocytes' that were confused with histiocytic lymphoma, with both cell types distinguishable from leukemic blasts; (2) patients who had undergone neurosurgical procedures, whose specimens sometimes had very atypical large cells but with the infiltrates more polymorphous than most histiocytic lymphomas and (3) chemotherapy-induced changes, including cellular degeneration and reactive histiocytosis, that could be distinguished from residual neoplastic cells by comparison with the patient's pretreatment fluids. We conclude that a primary diagnosis of leukemia or lymphoma on CSF should be made with caution. With appropriate history, knowledge of the morphology and behavior of a patient's particular type of lymphoma or leukemia can usually prevent incorrect diagnostic interpretations. (no Refs)

17. STATE OF LYMPHADENOID PHARYNGEAL RING IN PATIENTS WITH LYMPHOSARCOMA.

Belousova NV

Dept. Endoscopy, All-Union Cancer Res. Center, Moscow, USSR

Vestn Otorinolaringol; (5):44-47 1981

The results of endoscopic examination of the pharyngeal ring in 188 patients (aged 4 to 76 yr old) with lymphosarcoma are reported. Indications to endoscopy were functional disorders of the upper respiratory airways or/and enlargement of the neck lymph nodes. Of 188 patients, 112 were found to have primary lymphosarcoma of the pharynx, 29 had nontumoral diseases, and 47 were free of pathology of the upper respiratory airways. The greatest difficulties were encountered in differential diagnosis between primary lymphosarcoma and hyperplasia of the tonsil. Correct endoscopic diagnosis was made in 94.7% of the patients (false negative and false positive findings were recorded in 2.1% and in 3.2% of the patients, respectively). (16 Refs) (In RUS)

18. PRIMARY GASTRIC LYMPHOMA (MEETING ABSTRACT).

Weingrad D, Lightdale C, De Cosse J, Fillipa D, Sherlock P

Departments of Medicine, Surgery, and Pathology, Memorial Sloan-Kettering Cancer Center, New York, NY

Gastroenterology; 80(5,part2):1140 1981

The records of 46 patients with localized primary gastric lymphomas were reviewed and clinical and prognostic factors were characterized. The av age at presentation was 58 yr. The most common presenting symptoms were abdominal pain (84%) and wt loss (71%). Melena occurred in 24% and hematemesis in 6%. Laboratory evaluation yielded anemia in 41% and positive stool guaiacs in 43%. Upper gastrointestinal series showed ulcerations (39%), mass (71%) and infiltration (20%). Recurrence data after initial therapy showed 19/20 recurrences (95%) occurring in less than 24 mo with a mean of 12 mo. Overall survival was 57% 2 yr and 47% 5 yr. Sex breakdown yielded 48% male vs 72% females no evidence of disease (NED) at 2 yr. Age analysis showed less than 45 (71%) vs 45-65 (45%) vs greater than 65 (33%) NED at 2 yr. Tumor size vs survival showed: less than 5 cm (88%) vs 5-10 cm (50%) vs greater than 10 cm (48%). Survival vs stage showed Stage I (86%) vs Stage II (41%). Survival for surgery only vs surgery/radiation therapy combined revealed 59% vs 58% respectively. Analysis combining staging and therapy revealed Stage I surgery only (88%) vs Stage I surgery/radiation therapy (83%) vs Stage II surgery only (28%) vs Stage II surgery/radiation therapy (48%). In summary, female sex and younger age were associated with better survival postsurgery in primary gastric lymphoma, as were smaller tumor size, more localized stage and well-differentiated histology. The addition of abdominal radiation theray was of possible benefit only in Stage II disease. (no Refs)

19. NON HODGKIN LYMPHOMAS: PATTERNS OF HEPATIC INFILTRATION (MEETING ABSTRACT).

Rugge M, Fassina AS, Arslan-Pagnini C, Realdi G, Chieco Bianchi L
Institute of Pathological Anatomy, University of Padua, Padua, Italy
Eighth European Congress of Pathology, August 30-September 4, 1981, Helsinki, Finland. The Congress 92 pp., 1981.

Forty-three cases of non Hodgkin lymphoma (L) with hepatic infiltration were studied. Malignant lymphoma diagnosis was based on lymph node biopsy. According to the Kiel classification, malignant lymphomas were classified as either high or low grade malignancies consisting of Centroblastic Centocytic L (13 cases); Centroblastic L (7); Lymphoblastic L (7); Lewis Lung Carcinoma (6); Immunoblastic L (2); Lymphoplasmocytoid L (2); Centrocytic L (2); hairy lymphocytic leukemia (1); Mycosis Fungoides (1) and Malignant Histiocytosis (1). On histology three different patterns of hepatic lymphomatous infiltration were observed: 1) portal infiltration; 2) portal and lobular infiltration without lobular architectural effacement; 3) replacement of hepatic tissue by nodular lymphomatous infiltrates. Type 3 infiltration is found mostly in high grade malignant lymphomas. In low grade malignant lymphomas the hepatic architectural design is frequently well preserved and lymphomatous infiltration is usually type 1 and/or 2. (no Refs)

20. TESTICULAR LYMPHOMAS: A CLINICOPATHOLOGIC STUDY OF 35 CASES.

Turner RR, Colby TV, MacKintosh FR
Dept. Pathology, Stanford Univ. Medical Center, Stanford, CA, 94305
Cancer; 48(9):2095-2102 1981

Thirty-five patients with malignant lymphoma of the testis were reviewed. The lymphomas were classified by the Rappaport criteria and the recently introduced Working Formulation of non-Hodgkin's Lymphomas. The great majority of cases were diffuse histiocytic lymphoma (Rappaport), and these could be further subclassified by the Working Formulation. Significant differences in survival were observed between histologic subgroups of the Working Formulation and this effect was independent of stage, which also had a significant effect on survival. Of 23 clinically evaluable patients who presented with testicular lymphoma, 8 of 17 patients with intermediate-grade lymphomas are alive and well, in contrast to none of six patients with high-grade lesions. The recognition of histologic subtype as a prognostic factor independent of clinical stage is important for postorchiectomy management of these patients. (Author abstract) (22 Refs)

21. SKIN IMPRINT CYTOLOGY IN THE DIAGNOSIS OF CUTANEOUS T-CELL LYMPHOMAS (MEETING ABSTRACT).

Rosen SE, Koprowska I, Vonderheid EC
Department of Pathology, Temple University Hospital, Philadelphia, PA
Twenty-ninth Annual Scientific Meeting of the American Society of Cytology, November 2-7, 1981, St. Louis, Missouri. The Society 90 pp., 1981.

The early diagnosis of cutaneous T-cell lymphomas (CTCL) is difficult. Diagnostic criteria for early skin and lymph node involvement are not well defined, and recognition of the abnormal cerebriform lymphocte, while diagnostically helpful, may be difficult in tissue sections. A study of touch imprint cytology in the diagnosis of CTCL was begun with the following aims: 1) to evaluate the accuracy of the imprint technique: 2) to better characterize cytologic findings in early and late lesions of CTCL; and 3) as a long-term goal, to improve cytologic criteria for the early diagnosis of CTCL. This is a preliminary report of the study. Touch imprints were made on nine skin biopsies and two lymph nodes in which there was clinical suspicion of CTCL. Specimens were fixed in alcohol and stained by the Papanicolaou technique. Imprints from a variety of inflammatory dermatoses were used as controls. Cytologic and histologic interpretations were compared. The cytologic diagnosis was positive for mycosis fungoides (MF) in two cases suggestive of MF in four, and negative in three cases. These results correlated with the histologic diagnoses. Skin imprints from cases diagnosed as MF showed moderate to marked cellularity with a preponderance of lymphocytic cells and rare cerebriform cells. Skin imprint cytology appeared to be a reliable method in the diagnosis of CTCL in these cases. Cellular morphology and ability to identify cerebriform cells was enhanced by the Papanicolaou technique. (no Refs)

22. MALIGNANT SKIN LYMPHOMA: OLD HYPOTHESES AND RECENT CONCEPTS.

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MMW; 123(35):1291-1296 1981

The recent development of new concepts in cutaneous malignant lymphoma is reviewed. Malignant reticulopathies according to the old terminology are now classified as cutaneous T-cell and B-cell lymphoma, cutaneous leukemia (lymphocytic, myelocytic, and monocytic leukemias), cutaneous histiocytoses, and cutaneous Hodgkin's disease. The frequency of cutaneous non-Hodgkin's lymphomas of low-grade and high-grade malignancy was studied on the basis of three different series. Among the non-Hodgkin's lymphomas of low-grade malignancy, mycosis fungoides accounted for 20-30%, Sezary's syndrome for 4-9%, B-cell type chronic lymphocytic leukemia (CLL) for 0.3-16%, T-cell type CLL for 0.7-3%, immunocytoma for 6-22%, centrocytic lymphoma for 5-9%, and centroblastic-centrocytic lymphoma for 1.5-13%. Among the unclassified and high-grade cutaneous non-Hodgkin's lymphomas, centroblastic lymphoma accounted for 1.5-6%, immunoblastic lymphoma for 4-12%, lymphoblastic lymphoma for 3-8%, and unclassified lymphoma for 10-16%. (no Refs) (In GER)

MALIGNANT LYMPHOMA: CLINICAL IMMUNOLOGY AND IMMUNOTHERAPY

23. IMMUNOLOGIC SUBSETS IN HUMAN B-CELL LYMPHOMAS IN RELATION TO NORMAL B-CELL DEVELOPMENT.

Godal T, Lindmo T, Ruud E, Heikkila R, Henriksen A, Steen HB, Marton PF

Norsk Hydro's Inst. for Cancer Res., Montebello, Oslo 3, Norway

Haematol Blood Transfus; 26:314-319 1981

The expression of surface immunoglobulins (Igs), complement receptors, and Ig heavy chains on lymphocytic, centroblastic, centroblastic/centrocytic, and lymphoplasmacytoid lymphomas is reported. All the lymphomas could be triggered to differentiate and synthesize Ig in vitro by anti-Ig in com bination with tetradecanoylphorbol acetate. (20 Refs)

24. MALIGNANT LYMPHOMA WITH DUAL B AND T CELL MARKERS. ANALYSIS OF THE NEOPLASTIC CELLS WITH MONOCLONAL ANTIBODIES DIRECTED AGAINST T CELL SUBSETS.

Aisenberg AC, Bloch KJ, Wilkes BM

Huntington Memorial Lab., Massachusetts General Hosp., Boston, MA, 02114

J Exp Med; 154(5):1709-1714 1981

A human malignant lymphoma with characteristics of both B and T cells is reported. Neoplastic lymphocytes from five patients were analyzed. B cell characteristics were indicated by demonstration of surface-bound immunoglobulin containing IgM heavy chains and kappa light chains, an Ia-like antigen, and complement receptors. T cell characteristics were indicated by reaction with monoclonal antibodies for detection of sheep RBC OKT11 receptors (all cases), normal peripheral blood T cell OKT 3 determinant (4 cases), and inducer/helper (OKT4) or cytotoxic/suppressor (OKT8) determinants (4 cases). Cells from two cases formed sheep RBC rosettes. The malignant cells all originated from B lymphocytes of the follicular center. The mechanism of development of cells with dual characteristics is uncertain, but may involve derepression of genetic material, transformation of a stem cell before divergence of B and T lymphocyte differentiation, or neoplastic expansion of a normal cell population that has dual markers. (25 Refs)

25. MONOCLONAL ANTIBODY AGAINST A BURKITT LYMPHOMA-ASSOCIATED ANTIGEN.

Wiels J, Fellous M, Tursz T

Laboratoire d'Immunologie Clinique, Institut Gustave-Roussy, 94800 Villejuif, France

Proc Natl Acad Sci USA; 78(10):6485-6488 1981

A monoclonal antibody, referred to as 38.13, was obtained by fusing murine myeloma cells with Lewis rat splenocytes sensitized with Daudi cells (human Burkitt lymphoma containing Epstein-Barr virus genome but lacking HLA-A, -B, and -C and beta2-microglobulin molecules at the cell surface). 38.13 antibody was demonstrated to be a rat IgM. By complement-dependent microcytotoxicity and indirect immunofluorescence assays, 38.13 antibody was shown to react specifically with cells derived from Burkitt tumors, including both Epstein-Barr virus genome-carrying and Epstein-Barr virus-negative Burkitt lymphoma. By contrast, Epstein-Barr virus-containing lymphoblastoid cell lines derived from normal B lymphocytes were not recognized by 38.13 antibody. Fresh malignant cells from patients affected with various lymphoproliferative disorders were negative, except 4/8 having abdominal Burkitt-like lymphomas. Normal lymphocytes from peripheral blood, spleen, lymph node, tonsil, and bone marrow and mitogen (phytohemagglutinin, pokeweed mitogen, and concanavalin A)-activated blasts were also negative. Thus, 38.13 antibody apparently recognized a Burkitt-associated antigen that is not related to Epstein-Barr virus. The patter n of reactivity of 38.13 antibody with various Burkitt lymphoma cells appeared quite heterogenous and some Burkitt cells were consistently negative. 38.13 antibody thus defines a subset of Burkitt lymphomas. (Author abstract) (18 Refs)

26. COMPARISON OF HISTOLOGIC AND IMMUNOLOGIC HETEROGENEITY OF NON-HODGKIN'S LYMPHOMAS.

Borowitz MJ, Croker BP, Metzgar RS

Dept. Pathology, Duke Univ. Medical Center, Box 3712, Durham, NC, 27710

Am J Pathol; 105(2):97-106 1981

The lymphocyte surface marker phenotype in 11 selected cases of non-Hodgkin's lymphomas was determined with anti-Ig and mouse monoclonal antibodies against human lymphocyte antigens. A complement-mediated cell cytotoxicity assay on suspensions of the tumor cells was compared with an indirect immunoperoxidase technique on frozen tissue sections. Both methods gave good results in tumors with a uniform cell population, but the frozen section technique was superior in heterogeneous tumors. The six B-cell neoplasms were heterogeneous with respect to expression of surface Ig and Ia antigens. The five T-cell tumors were morphologically heterogeneous and also highly variable in their expression of different T-cell specific antigens. (Author abstract) (33 Refs)

MALIGNANT LYMPHOMA: CHEMOTHERAPY

27. ACYCLOVIR TREATMENT OF EPSTEIN-BARR VIRUS (EBV) INDUCED POST-TRANSPLANT LYMPHOMA (MEETING ABSTRACT).

Hanto DW, Sakamoto K, Purtilo D, Balfour HH, Simmons RL, Najarian JS

University of Minnesota, Minneapolis, MN, 55455

Program and Abstracts of the 21st Interscience Conference on Antimicrobial Agents and Chemotherapy, November 4-6, 1981, Chicago, Illinois American Society for Microbiology; :A30 1981

Lymphoma occurs in 0.7% of renal transplant recipients and the mortality is high (90%). No effective therapy has been reported. Acyclovir (ACV) an anti-viral agent, has promise to this application in light of our evidence that EBV is the cause of these tumors. A transplant developed a tumor in lymph nodes, tonsils, and bone marrow. Cell markers showed a B cell proliferation producing Ig of polyclonal specificity (IgM, IgG, and IgG, kappa and lambda). Staining for EBV nuclear antigen was positive and cyclic RNA/DNA filter hybridization demonstrated 3 EBV genome equivalents per tumor cell. Oropharyngeal shedding of EBV was shown. ACV for 7 days resulted in a dramatic objective and subjective response; EBV shedding disappeared. Forty-eight hr after stopping ACV, fever, symptoms, and objective tumor growth recurred. A second ACV course resulted in resolution lasting 3 mo. A polyclonal B cell recurrence responded to ACV. One mo later a third recurrence, resistant to ACV, resulted in patient death. Cell markers demonstrated sIg/cIg of the IgG kappa class only. ACV is effective during the polyclonal growth phase of these EBV induced lymphom as. The tumor probably evolved into a monoclonal neoplasm which was resistant to ACV. This is the first documented in vivo effect of ACV on EBV. (no Refs)

28. NODULAR MIXED LYMPHOMA: RESULTS OF A RANDOMIZED TRIAL FAILING TO CONFIRM PROLONGED DISEASE-FREE SURVIVAL WITH COPP CHEMOTHERAPY.

Glick JH, Barnes JM, Ezdinli EZ, Berard CW, Orlow EL, Bennett JM
Hosp. Univ. Pennsylvania, 3400 Spruce St., Philadelphia, PA, 19104
Blood; 58(5):920-925 1981

Fifty-two patients with Stage III or IV nodular mixed lymphocytic-histiocytic lymphoma (NM) were entered on a prospective randomized trial comparing cyclophosphamide-prednisone (CP) to either COPP (cyclophosphamide, vincristine, procarbazine, prednisone) or BCVP (BCNU (1,3-bis(2-chloroethyl)-1-nitrosourea), cyclophosphamide, vincristine, prednisone). The COPP regimen utilized in this Eastern Cooperative Oncology Group (ECOG) trial was similar to the four-drug regimen C-MOPP reported by the NCI to achieve prolonged relapse-free survival in this histology. No significant differences in complete response rates, response duration, or overall survival were noted among the three regimens. A pattern of continuous late relapse was observed for all three chemotherapy programs. Although 11 of the 18 (61%) COPP patients achieved a complete response, only 3/11 (27%) remain disease-free with a median follow-up of over 3 yr. However, two of these three long-term complete responders have died with no clinical evidence of recurrent disease. The COPP patients received 84% of the calculated ideal doses of cyclophosphamide and 78% of the ideal dosage of procarbazine. Grade 3-4 hematologic toxicity was noted in 22% of the COPP group, 36% with BCVP, and 0% for the CP patients. We were unable to confirm the ability of COPP to achieve durable complete remissions in MN lymphoma. The cyclophosphamide-prednisone combination was equally effective when compared with COPP and BCVP, but produced minimal toxicity. (Author abstract) (17 Refs)

29. HIGH-DOSE COMBINATION CHEMOTHERAPY FOR NON-HODGKIN'S LYMPHOMA OF UNFAVOURABLE HISTOLOGICAL TYPE (MEETING ABSTRACT).

Bell R, Gallagher CJ, Ford J, Malpas JS, Lister TA
ICRF Department of Medical Oncology, St. Bartholomew's Hospital, London EC1, England
Br J Cancer; 43(5):720 1981

Twenty-one consecutive untreated patients (pts) with non-Hodgkin's lymphoma (NHL) of unfavorable histology were treated between May 1978 and August 1979. Fifteen males and 6 females, median age 55 yr old (range 18-70) were of the following histological groups (Rappaport) diffuse histiocytic 15, diffuse undifferentiated 6, immunoblastic 8, lymphoblastic 3, centroblastic 3, malignant histiocytosis 3 and other high-grade 4. All but one had Stage IV disease. High-dose combination chemotherapy was given as cyclophosphamide 2.5 g/m2 iv, Adriamycin 50 mg/m2 iv, vincristine 2 mg iv, methotrexate 12.5 mg intrathecal and daily prednisolone 1 g/m2 iv x 5, repeated every 3-4 wk for a minimum of 6 courses. There were 7 responders (33% overall) of which 4 were complete responses (CR) 2 partial responses with minimal x-ray abnormalities and one failure who entered CR after cranial and abdominal radiotherapy. All responders are alive without relapse for a mean period of 17.0 mo (range 12-24.7) with a mean duration of remission of 10.6 mo (range 6.2-14). Six pts failed to respond and died with resistant disease and infection. Four pts died of infection during remission induction with responding disease, and four others died in the first cycle of treatment, one of infection, one of gastric hemorrhage, one of myocardial infarction and one of severe metabolic disturbance. A more intensive program has doubled the survival (33%) of our Stage IV unfavorable histology pts. (1 Ref)

30. PHASE II TRIAL OF CIS-DICHLORODIAMMINEPLATINUM (II) IN ADVANCED MALIGNANT LYMPHOMA: A STUDY OF THE CANCER AND ACUTE LEUKEMIA GROUP B.

Cavalli F, Jungi WF, Nissen NI, Pajak TF, Coleman M, Holland JF
Div. Oncology, Ospedale San Giovanni, 6500 Bellinzona, Switzerland
Cancer; 48(9):1927-1930 1981

In a cooperative study of the Cancer and Acute Leukemia Group B, 27 evaluable patients with advanced malignant lymphomas were treated with 70 mg/m2 of cis-dichlorodiammineplatinum(II) (cis-platinum) once every 3 wk. All patients had received extensive prior therapy. Partial remission was obtained in 2 of 8 patients (25%) with Hodgkin's disease, for 6 and 40 wk, and in 5 of 19 (26%) patients with non-Hodgkin's lymphoma, for a median duration of 6 wk. The major toxic effects were profuse vomiting and, to a lesser degree, myelosuppression. Nephrotoxicity was easily controlled, Cis-platinum is an active agent in lymphoma and should merit incorporation into combination therapy for recently diagnosed disease. (Author abstract) (10 Refs)

MALIGNANT LYMPHOMA: RADIOTHERAPY

31. TOTAL-BODY IRRADIATION IN ADVANCED NON-HODGKIN'S LYMPHOMA (MEETING ABSTRACT).

Dobbs HJ
Department of Radiotherapy, Royal Marsden Hospital, Sutton, Surrey SM2 5PT, England
Br J Radiol; 54(640):371 1981

Total body irradiation (TBI) has been shown in a randomized trial to give similar response and survival rates to combination chemotherapy in the treatment of lymphomas. Between 1973 and 1977, 37 patients with Stage III and IV non-Hodgkin's lymphomas were treated at the Royal Marsden Hospital. Twenty-four patients had received no previous therapy. Patients with nodular lymphoma were treated on evidence of progressive disease. TBI of 1.5 Gray (Gy) (150 rad) max permissible dose (MPD) and 12 days or ten fractions treating twice weekly. Eleven patients received hemibody irradiation of 3 Gy (300 rad) MPD in ten fractions an d 12 days. The complete response rate in 22 patients with nodular lymphoma was 64% compared to 40% in the 15 patients with diffuse disease. The overall response rate was 73% for the nodular and 80% for the diffuse lymphomas. The medium duration of response was 12 mo. Bone marrow toxicity was the major complication but there was no incidence of serious hemorrhage. Fourteen out of 37 (38%) of patients had platelet counts less than 50000/mm3 and in six of these no further chemotherapy was possible. All six had involvement of the bone marrow and five of them had received hemibody irradiation. The overall response rate of 76% is similar to that achieved with chemotherapy and is without serious toxicity. Subsequent chemotherapy was given successfully except in those patients with prolonged thrombocytopenia which appeared to be related to an involved bone marrow. (no Refs)

32. WHOLE BODY IRRADIATION IN NON-HODGKIN'S LYMPHOMA (MEETING ABSTRACT).

Bullimore JA
Radiotherapy Centre, Bristol Royal Infirmary, Bristol, England
Br J Radiol; 54(640):371 1981

Twenty-six patients with non-Hodgkin's lymphoma, unresponsive to or in relapse following chemotherapy, received total-body irradiation (TBI) to a dose of 150 centiGray (rad) in 15 fractions over 18 days. A response was achieved with 17 patients, in six of whom it was complete. The actuarial survival rates were 50% at one yr and 42% at 30 mo. Best results were achieved in those with low-grade histology and in those under 60 yr of age. Transient marrow toxicity was the only significant side-effect of treatment; although it was usually severe, there were no serious sequelae. TBI should be considered as a secondary therapy in non-Hodgkin's lymphoma, regardless of previous treatment. (no Refs)

33. NON-HODGKIN'S MALIGNANT LYMPHOMAS OF UPPER DIGESTIVE AND RESPIRATORY TRACTS.

Plantenga KF, Hart H, Van Heerde P, Tierie AH
(c/o Tierie) Dept. Radiation Therapy, Free Univ., De Boelelaan 1105, 1007 MB Amsterdam, The Netherlands
Int J Radiat Oncol Biol Phys; 7(10):1419-1427 1981

Radiation therapy (RT) was given to 91/102 patients with non-Hodgkin's lymphoma involving the upper digestive and respiratory tracts. RT was given to 62 at sites of involvement only; 29 received elective RT of contiguous uninvolved areas. Other prior treatment included surgery (3) and chemotherapy (8). Complete remissions (CR) were obtained in 72/82 Stage I and II patients. Of the nine initial failures, no correlation was found to site of origin or histology, although most were bulky lesions. Among the 72 with CR, 36 relapsed during the first yr. Av survival was 14 mo for all stages. Survival at 5 yr was 28% for Stage I and 12% for Stage II. According to the Rappaport classification, those with the histiocytic poorly differentiated tumors had a poorer prognosis than the other types. With the Lukes and Collins classification, small and large cleaved lymphomas did significantly better than large non-cleaved, immunoblastic and small cleaved lymphomas ($p = 0.006$). According to the Lennert classification, low grade lymphomas had a significantly longer tumor-free period than high grade lymphomas. Radiation doses between 4,000 and 5,000 rad also showed a longer tumor-free period compared to lower doses. Adjuvant chemotherapy is recommended in Stages I and II after primary RT because of the high rate of primary relapse in distant sites. (21 Refs)

MALIGNANT LYMPHOMA: CASE REPORTS

34. FOCAL LYMPHOID HYPERPLASIA OF THE STOMACH PRECEDING GASTRIC LYMPHOMA: CASE REPORT AND REVIEW OF THE LITERATURE.

Wolf JA, Spjut HJ
(c/o Spjut) Dept. Pathology, Baylor Coll. Medicine, Texas Medical Center, Houston, TX, 77030
Cancer; 48(11):2518-2523 1981

A case is reported in which focal lymphoid hyperplasia (pseudolymphoma) of the stomach preceded by 45 mo the development of gastric diffuse lymphocytic lymphoma. Review of the literature discloses only two similar cases reported with satisfactory histopathologic documentation. Analogous cases, in other anatomic sites, of an apparent association between benign and malignant lymphoid lesions are reviewed. The cases suggest that occasionally lymphoid hyperplasia of the stomach may precede lymphoma. Lymphoid hyperplasia is not yet considered a consistent precursor of lymphoma. (Author abstract) (46 Refs)

35. SIGNET RING CELL LYMPHOMA: A RARE VARIANT OF FOLLICULAR LYMPHOMA.

Harris M, Eyden B, Read G
Dept. Pathology, Christie Hosp., Holt Radium Inst., Manchester M20 9BX, England
J Clin Pathol; 34(8):884-891 1981

A case of signet ring cell lymphoma, the eighth in published reports is recorded. This rare tumor is a variant of follicular lymphoma which may be mistaken for metastatic carcinoma. The case has been studied by light microscopy, immunohistochemistry and electron microscopy and confirms that this sub-group has rather uniform characteristics. Observations on the possible origins of the vacuoles are presented. (Author abstract) (10 Refs)

MALIGNANT LYMPHOMA: SELECTED REPORTS ON ETIOLOGY AND EPIDEMIOLOGY

36. ANTIBODIES IN HUMAN SERA REACTIVE AGAINST AN INTERNAL STRUCTURAL PROTEIN OF HUMAN T-CELL LYMPHOMA VIRUS.

Kalyanaraman VS, Sarngadharan MG, Bunn PA, Minna JD, Gallo RC
(c/o Gallo) Lab. Tumor Cell Biology, NCI, Bethesda, MD, 20205
Nature; 294(5838):271-273 1981

A limited survey was designed to determine whether natural antibodies reactive against the human retrovirus isolate, HTLV, can be detected in human sera. The assay involved use of a radioimmune precipitation of 125I-labeled HTLV-cr p24 by human sera using a double antibody system. The p24 of HTLV-cr was purified to homogeneity from density-banded virus and radiolabeled with 125I. Serum from patient CR (the source of the isolate) and serum from another patient, MJ, with Sezary syndrome showed high reactivity to HTLV-cr p24. Twenty-one sera from various T-cell malignancies and 50 sera from random normal donors showed no significant precipitating activity. Eleven sera from close family members of patients with T-cell malignancies and previous evidence of HTLV infection were studied. Only one, from the wife of patient CR, reacted strongly in the immunoprecipitation. The antibodies against p24 are present in human sera, and these are specifically directed at HTLV-cr proteins and not at cell-specific determinants. Thus, the immunological reactions are not those reported in human sera against animal virus glycoproteins which, lacking virus specificity, are directed against the carbohydrate residues of the glycoprotein. The antibodies against HTLV are thus the first evidence for a specific immune response in humans against a retrovirus. (15 Refs)

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HODGKIN'S DISEASE: CLINICAL IMMUNOLOGY AND IMMUNOTHERAPY

1. CELLULAR AND HUMORAL IMMUNITY IN HODGKIN'S DISEASE: I. PATIENTS IN CONTINUOUS LONG-TERM REMISSION.

Skovmann-Sorensen O, Schroder H, Moller-Larsen A, Haahr S

(c/o Haahr) Inst. Medical Microbiology, Univ. Aarhus, Bartholin Building, DK-8000 Aarhus C, Denmark

Scand J Haematol; 27(3):171-180 1981

Cell-mediated and humoral immunity to herpes simplex virus (HSV), cytomegalovirus (CMV) and varicella zoster virus (VZV) were examined in 37 patients with Hodgkin's disease in continuous long term remission. This group had lower blast-transformation than a matched control group to all three antigens. Patients originally showing B-symptoms had higher transformation to VZV than those with A-symptoms. Patients treated with irradiation only had higher transformation than those treated with either chemotherapy or a combination of chemotherapy and irradiation. There was a clear tendency towards lower transformation in patients having been in remission for 2 yr or less. Phytohemagglutinin (PHA) stimulation gave lower response in the patient group than in the control group. Patients with B-symptoms had lower response than those with A-symptoms. Interferon production was specially impaired in patients with B-symptoms. The patient group had higher CF titers against HSV and CMV while the control group had higher titers against VZV. B-symptom patients had higher titers against VZV than A-symptom patients. It is concluded that HD patients have impaired immune function many years after discontinuation of therapy, but there are certain differences regarding the in vitro immunity within the patient groups. (Author abstract) (17 Refs)

2. IMPAIRED B-LYMPHOCYTE REACTIVITY IN PATIENTS WITH HODGKIN'S DISEASE AND NON-HODGKIN-LYMPHOMAS.

Ruhl H, Enders B, Bur M, Sieber G

Klinikum Steglitz der freien Universitat Berlin, Hematologische Abteilung, Hindenburgdamm 30, D-1000 Berlin 45, W. Germany

Blut; 42(5):271-281 1981

The ability of B cells to differentiate into immunoglobulin-secreting cells (ISC) was studied by a reverse hemolytic plaque assay in 42 patients with Hodgkin's disease (HD) and 33 patients with non-Hodgkin lymphomas (NHL). Forty healthy individuals served as controls. Induction of ISC was triggered by pokeweed mitogen, with optimum response in all groups at concentrations of 1.0-15.0 ul/ml. Mean numbers of ISC (x 10(-2)/10(6) peripheral blood lymphocytes) were 4,370 for HD patients and 2,450 for NHL patients. Mean control value was 10,540. Most HD and NHL patients showed reduced response. No clear correlation between response and patient age could be demonstrated. Response in HD patients decreased with progression of disease, although most patients in remission were still below normal. Coculturing of HD or NHL lymphocytes with normal lymphocytes indicated the NHL response deficiency was due to a B cell defect, T cell function being normal. HD deficiency was due to a B cell defect plus defects in T helper cells and suppressor cells. HD deficiency is evidently reversible and can be corrected with appropriate therapy. (38 Refs)

3. CONCENTRATION OF ROSETTE-FORMING CELLS AND FUNCTIONAL ACTIVITY OF PERIPHERAL BLOOD T-LYMPHOCYTES IN DIFFERENT STAGES OF HODGKIN'S DISEASE.

Loseva MI, Fridliand DIu
Dept. Therapy, Faculty Pediatrics, Medical Inst., Novosibirsk, USSR
Ter Arkh; 53(9):68-71 1981

Functional activity of peripheral blood lymphocytes was studied in 75 Hodgkin's disease patients (56% men, 44% women; median age group, 20-29 yr). Among these patients, 28 had Stage II disease, 28 had Stage III, and 19 had Stage IV. Prior to polychemotherapy, concentrations of T-rosette-forming cells in the Stage II, III, and IV patients were 29.6%, 24.1%, and 19.3%, respectively; macrophage migration indices were 54.9%, 61.3%, and 69.0%, respectively. The contents of B lymphocytes showed progressive increases from 20.1% for Stage II disease to 28.7% for Stage III and 29.5% for Stage IV. Polychemotherapy resulted in certain normalization of the immunological indices; however, during remission, the patients developed secondary imbalance of the content of immunocompetent cells. (8 Refs) (In RUS)

HODGKIN'S DISEASE: CHEMOTHERAPY

4. PHASE II STUDY OF HEXAMETHYLMELAMINE IN REFRACTORY HODGKIN'S DISEASE, OTHER LYMPHOMAS, AND CHRONIC LYMPHOCYTIC LEUKEMIA.

Southeastern Cancer Study Group
(c/o G. Omura) Dept. Medicine, Div. Hematology and Oncology, Univ. Alabama, 638 Zeigler Building, University Station, Birmingham, AL, 35294
Cancer Treat Rep; 65(11/12):1027-1029 1981

A long-term daily dose of hexamethylmelamine was tested in patients with Hodgkin's disease, nodular and diffuse lymphomas, and chronic lymphocytic leukemia who had failed conventional treatment. There were no responses among 20 patients with chronic lymphocytic leukemia, 12 with nodular lymphomas, and 11 with diffuse well-differentiated lymphocytic lymphomas. However, 5 of 24 patients with Hodgkin's disease (21%) responded and 7 of 36 (19%) with diffuse lymphomas other than diffuse well-differentiated lymphocytic lymphomas responded. This new agent is active in selected histologic types of lymphoma. (Author abstract) (4 Refs)

HODGKIN'S DISEASE: RADIOTHERAPY

5. THYMIC CYSTS FOLLOWING RADIATION THERAPY FOR HODGKIN DISEASE.

Baron RL, Sagel SS, Baglan RJ
Dept. Radiology, Hosp. Univ. Pennsylvania, Philadelphia, PA
Radiology; 141(3,part1):593-597 1981

In three patients, benign thymic cysts developed following radiation therapy for Hodgkin disease. Autopsy or surgical specimens provided a diagnosis in all three cases; computed tomographic (CT) scans obtained in two of the patients provided a preoperative diagnosis. The etiology of these cysts is uncertain; they may arise following successful radiation treatment of Hodgkin disease involving the thymus. When an anterior mediastinal mass develops in a patient with Hodgkin disease following radiation therapy, careful evaluation to exclude a benign process is indicated prior to initiating additional therapy. (Author abstract) (11 Refs)

HODGKIN'S DISEASE: MULTIMODAL THERAPY

6. THE TREATMENT OF ADVANCED HODGKIN'S DISEASE.

Straus DJ, Lee BJ, Koziner B, Nisce LZ, Young CW, Clarkson BD
Hematology-Lymphoma Service, Dept. Medicine, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Blut; 43(2):119-124 1981

Of 118 patients treated for advanced Hodgkin's disease (HD) with 8 mo of alternating MOPP (nitrogen mustard, vincristine, procarbazine, and prednisone) and ABDV (adriamycin, bleomycin, dacarbazine, and vinblastine) and low dose radiotherapy (2,000 rad tumor dose), 91 (54 males, 37 females; 16-64 yr old) were evaluable. Fifty-seven patients had nodular sclerosis, 25 mixed cellularity, and 9 not subclassified histologies. Fifteen patients were Stage IIB, 13 Stage IIIA, 28 Stage IIIB, and 35 Stage IV. Among evaluable previously-untreated patients (PU), 50/57 achieved complete remission (CR) and 7/57 partial remission (PR). In minimally pretreated (MP) patients, CR was obtained in 11/16, PR in 3/16, and no response in 2/16. Among heavily-pretreated (HP) patients, 9/18 achieved CR, 4/18 PR, and 5/18 failed to respond. Differences in response rates between patients in each stage for PU or MP patients were not statistically significant. Overall, there were 15 relapses among CR patients, 6 among PU, 3 among MP, and 6 among HP patients. Severe nausea and vomiting particularly related to dacarbazine and nitrogen mustard administration occured in all patients; therapy was discontinued in 13 patients due to the severity of these side effects. Other complications include acute leukemia (1), pulmonary disorders (6), cardiomyopathy (1), acute pericarditis (1), peripheral neuropathy (2), and aseptic bone necrosis (2). Of 35/118 patients who died, 31 died from HD, 2 from second malignancies, 1 from pneumococcal meningitis, and 1 from graft-versus-host disease. The above results are the best reported for the treatment of advanced HD. (10 Refs)

7. TREATMENT OF STAGE I AND II MEDIASTINAL HODGKIN DISEASE. A COMPARISON OF INVOLVED FIELDS, EXTENDED FIELDS, AND INVOLVED FIELDS FOLLOWED BY MOPP IN PATIENTS STAGED BY LAPAROTOMY.

Hagemeister FB, Fuller LM, Sullivan JA, North L, Velasquez W, Conrad FG, McLaughlin P, Butler JJ, Shullenberger CC
Dept. Internal Medicine, Section Hematology, M. D. Anderson Hosp. and Tumor Inst., Univ. Texas System Cancer Center, 6723 Bertner Ave., Houston, TX, 77030
Radiology; 141(3,part1):783-789 1981

Three treatment programs for Stage I and II mediastinal Hodgkin disease (established by laparotomy) were compared. Involved-field radiotherapy plus MOPP gave a disease-free survival rate of 97%, significantly different from 62% and 55% for involved and extended fields, respectively. Corresponding survival figures of 97%, 88%, and 84% were not significantly different statistically due to salvage with radiotherapy and/or chemotherapy. Among patients given radiotherapy alone, the survival figure of 94 % for limited mediastinal disease was significantly better than 63% for extensive mediastinal and hilar disease; corresponding disease-free figures of 72% and 35% were also significantly different. Constitutional symptoms were an important prognostic factor in disease-free survival following the use of involved fields; hilar disease was important only with large mediastinal masses. Most relapses were intrathoracic; MOPP alone salvaged only 47%. Treatment of Stage I and II Hodgkin disease should be based on symptoms, extent of mediastinal disease, and hilar involvement. (Author abstract) (26 Refs)

8. COMBINED RADIO- AND CHEMOTHERAPY IN PATIENTS WITH STAGE I-II HODGKIN'S DISEASE.

Baisogolov GD, Khmelevskaia ZI, Shakhtarina SV
Inst. Medical Radiology, Obninsk, USSR
Ter Arkh; 53(9):144-146 1981

The efficacy of polychemotherapy using cyclophosphamide, oncovin or vinblastine, procarbazine, and prednisone (COPP or CVPP regimens) in combination with irradiation of the regional lymph nodes and the spleen (4,000-4,500 rads in 4 wk to primary tumor and 3,500 rads in 3 wk to regional lymph nodes) was evaluated in 90 patients with Stage I-II Hodgkin's disease. The patients were followed up for 2 yr: 1 patient died, 6 developed recurrences, and 83 were recurrence-free. (15 Refs) (In RUS)

HODGKIN'S DISEASE: SELECTED REPORTS ON ETIOLOGY AND EPIDEMIOLOGY

9. TONSILLECTOMY: A PROGNOSTIC FACTOR IN HODGKIN'S DISEASE?

Gobbi PG, Cavalli P, Franzini B, Di Prisco U, Federico M, Bonacorsi G
Istituto di Patologia Medica 1, Policlinico S. Matteo, 27100 Pavia, Italia
Tumori; 67(5):425-430 1981

The clinical features and course of Hodgkin's disease (HD) were investigated in 160 previously tonsillectomized patients and compared with 375 nontonsillectomized ones. In both groups, sex, social class, histologic type, stage and symptoms were almost identically distributed. Tonsillectomized patients showed a higher incidence of initial cervical forms (p less than 0.05) and more frequently developed the disease under 35 yr of age (p less than 0.001), thus also reflecting the different policies of the otolaryngologists in the past few decades. Moreover, the tonsillectomized patients enjoyed a significantly better survival (p = approx 0.01) than the nontonsillectomized ones. Adjusted survival curves for age and site of initial involvement proved that the favorable prognostic value of tonsillectomy was not due to the altered distribution of these two factors in the two groups; in addition, an earlier diagnosis in tonsillectomized patients could be excluded. The favorable effect of tonsillectomy in HD patients might be related specifically to the reduced portion of immunologically reacting oropharyngeal lymphoid tissue remaining after tonsillectomy. A decreased output of the specific immune-complexes, which are responsible for the disease, according to Vianna's theory, might be hypothesized in tonsillectomized patients. (Author abstract) (30 Refs)

MALIGNANT LYMPHOMA: DIAGNOSIS AND STAGING

10. DIAGNOSTIC PROBLEMS IN THE CYTOLOGIC EVALUATION OF CEREBROSPINAL FLUID FOR LYMPHOMA AND LEUKEMIA.

Borowitz M, Bigner SH, Johnston WW
Dept. Pathology, Duke Univ. Medical Center, Box 3712, Durham, NC, 27710
Acta Cytol (Baltimore); 25(6):665-674 1981

We reviewed 72 cerebrospinal fluid (CSF) specimens with abnormal hematopoietic cells and the clinical records of the 45 patients from whom they were obtained. Of the 72 specimens, 34 were originally diagnosed as positive for lymphoma or leukemia and the remaining 38 as 'atypical cells present.' Based on follow-up information of the patients, only 3 'atypical' specimens were from patients with CSF leukemia, but 10 of the positive diagnoses were incorrect. Cases of acute lymphoblastic leukemia (ALL) produced cells with a characteristic morphology. Cells of five of the six false-positive specimens in this disorder were, in retrospect, markedly different from typical blasts. In contrast, two false-positive reactive cases from patients with no established malignancy had an infiltrate whose morphology was indistinguishable from that of many cases of diffuse histiocytic lymphoma (DHL). There were no cases of chronic lymphocytic leukemia (CLL) or nodular poorly differentiated lymphocytic lymphoma involving CSF, but two patients with CLL and infectious meningitis had false-positive cytologies. We conclude that in evaluating CSF specimens for lymphoma or leukemia, knowledge of the morphology and behavior of a patient's particular tumor can minimize incorrect diagnostic interpretations. (Author abstract) (16 Refs)

11. HISTOLOGIC VARIATION IN NON-HODGKIN'S LYMPHOMAS: COMMENTARY.

Hoppe RT
Div. Radiation Therapy, Dept. Radiology, Stanford Univ. Medical Center, Stanford, CA, 94305
Cancer Treat Rep; 65(11/12):935-939 1981

Incidence and natural history of the following histologic subtypes of non-Hodgkin's lymphomas are discussed: lymphomas with a mixed architectural pattern (nodular and diffuse areas in a single biopsy), composite lymphomas (variation in cell type within a single biopsy), discordant lymphomas (variation in histologic subtype in biopsies from different sites), lymphomas showing conversion to a new histologic type during the course of disease, and lymphomas with histologic changes documented only at autopsy. Current concepts of histologic conversion are detailed, including the possibility that some cases are treatment-related, and the risk of conversion among follicular lymphoma patients. (38 Refs)

12. NODULAR POORLY DIFFERENTIATED LYMPHOCYTIC LYMPHOMA: CHANGES IN HISTOLOGY AND SURVIVAL.

Ostrow SS, Diggs CH, Sutherland JC, Gustafson J, Wiernik PH
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Cancer Treat Rep; 65(11/12):929-933 1981

Lymphoma patients with a nodular pattern have a better prognosis than those with a diffuse pattern. histologic evolution from nodular to diffuse may occur during the course of the disease in the same patient. This change in pattern may be of prognostic significance. We reviewed 56 patients with an initial diagnosis of nodular poorly differentiated lymphoma seen over a 12-yr period (1966-1978). Thirty-five patients had biopsies after initial diagnosis, and 28 of the cases could be classified as nodular or diffuse. Eleven of the 56 cases evolved from a nodular to a diffuse pattern. Forty-four of the 56 patients achieved a complete remission and were evaluated for survival. The median survival (66+ mo) for patients who have never relapsed is similar to that for patients who relapsed with a nodular pattern (70 mo) and patients who relapsed with a diffuse pattern (73 mo). Relapse with a nodular pattern occurred at a median of 27 mo after initial diagnosis and relapse with a diffuse pattern occurred at a median of 49 mo. Although overall survival in patients relapsing with nodular or diffuse disease is similar, median survival from relapse with nodular disease is longer (32+ mo) than median survival with diffuse disease (17 mo) ($p = 0.068$). (Author abstract) (23 Refs)

13. LYMPHOPLASMACYTIC/LYMPHOPLASMACYTOID LYMPHOMA: A CLINICAL ENTITY DISTINCT FROM CHRONIC LYMPHOCYTIC LEUKAEMIA?

Heinz R, Stacher A, Pralle H, Theml H, Brunsvicker F, Burkert M, Common H H, Fulle H, Grisar t, Gruneisen A, Hermann F, Leopld H, Liffers R, Meusers P, Nowicki L, Nurnberg R, Rengshausen H, Ruhl U, Schoengen A, Schmidt M, Wirthmuller R, Schwarze E W, Brittinger g

Ludwig-Boltzmann-Institut fur Leukamieforschung und Hamatologie, Hanusch-Krankenhaus, Heinrich-Collin-Strasse 30, A-1140 Vienna, Austria

Blut; 43(3):183-192 1981

The clinical features and prognosis of 116 patients (34-84 yr old) with chronic lymphocytic leukemia (CLL) and 114 patients (27-86 yr old) with lymphoplasmacytic/lymphoplasmacytoid lymphoma (IC) are described. CLL and IC occurred most often in patients 60-90 yr old. Males predominated in both disorders with a male:female ratio of 1.76:1 in CLL and 1.47:1 in IC. IC constitutional (B) symptoms were nearly twice as frequent than in CLL (60.7% versus 36%). Most patients exhibited enlarged lymph nodes at diagnosis. Rapid lymph node enlargement was noted more frequently in IC patients than in CLL patients. All CLL patients were classified as Stage IV due to bone marrow infiltration. IC patients were classified as Stage IV due to bone marrow infiltration (90.7%) or liver and/or skin involvement (5%) or Stage I (5.2%). Peripheral blood lymphocytosis with lymphocyte counts exceeding 4,000/ul was observed in 94.8% of CLL patients and in 66.1% of IC patients. Alterations of total serum proteins and extranodal manifestations in CLL and IC patients are described. Criteria for onset of chemotherapy in Stage IV disease were fulfilled in 18% and 49% of CLL and IC patients, respectively. Of 19 CLL patients treated, 1 showed complete remission and 10 reached partial remission. In 18/46 IC patients, partial remission was achieved. The results indicated that histopathological differentiation of IC from CLL has some distinct clinical correlates which characterize IC the less favorable lymphoma entity. (30 Refs)

14. SURFACE MARKER IDENTIFICATION OF SMALL CLEAVED FOLLICULAR CENTER CELL LYMPHOMAS WITH A HIGHLY FAVORABLE PROGNOSIS.

Rudders RA, Ahl ET, Delellis RA, Bernstein S, Begg CB
New England Medical Center Hosp., 171 Harrison Ave., Boston, MA, 02111
Cancer Res; 42(1):349-353 1982

Between 1976 and 1980, 143 cases of non-Hodgkin's lymphoma have been prospectively analyzed for correlations between surface marker phenotype, histomorphology, and prognosis. This study analyzed 44 adults with tumors classified by Lukes-Collins criteria as small cleaved follicular center cell lymphomas. Two surface marker phenotypic subsets were studied based on the expression of either the second surface membrane Ig, IgD, or a receptor for the third component of the complement system (C'3) (Group I = IgD+ and/or C'3+, Group II = IgD-C'3-). Eleven of the 44 patients have died with a projected median survival of 58 mo. Four patients in Group I have died with a median survival of 58 mo while seven patients in Group II have died with a median survival of 30 mo. The difference in the survival curves for the two subgroups is statistically significant ($p = 0.01$). An analysis of variables such as stage, age, sex, and sites of involvement revealed no differences between the two groups. When classified histologically, the two groups were morphologically indistinguishable and had similar distributions of nodular (follicular) and diffuse variants. Of interest, five patients in Group I were judged to require no initial therapy whereas none in Group II remained untreated initially. The expression of the second heavy chain delta and/or a receptor for C'3 appears to define a subgroup of small cleaved follicular center cell lymphomas with an indolent course and an excellent prognosis. (Author abstract) (20 Refs)

15. GERMINAL CENTER CELL LYMPHOMAS: PROGNOSTIC SIGNIFICANCE OF THEIR HISTOPATHOLOGICAL DIFFERENTIATION.

Konig E, Bartels H, Bremer K, Burger-Schuler A, Common H, Duhmke E, Engelhard M, Fulle HH, Gunzer U, Koeppen KM, Leopold H, Nowicki L, Oertel G, Paetzmann S, Ruhl U, Schmidt M, Schoengen A, Scholle H, Stacher A, Wolf-Hornung B, Schwarze E W, Brittinger G
Div. Haematology, Dept. Medicine, Univ. Essen, Hufelandstrasse 55, D-4300 Essen, W. Germany
Blut; 43(3):193-200 1981

A prospective study of 195 patients with lymphomas originating from germinal center cells (48 CTL: centrocytic lymphoma; 83 CCL: centroblastic/centrocytic lymphoma; and 64 CBL: centroblastic lymphoma) examined the clinical and prognostic features of the Kiel classification system. The median age of CTL patients (62 yr) was approx 10 yr greater than than that of CCL patients. There was a strong preponderance of males over females in CTL, but of females over males in CCL. Of CCL and CTL patients, 24% and 38%, respectively, showed rapid lymph node enlargement. Atypical lymphocytes were seen in both CCL and CTL patients. Stages III and IV were seen in about 75% of patients suffering from CTL and CCL, but in only 56% of CBL patients. Initial bone marrow and liver infiltration was found in 63% and 4%, respectively, of CTL patients, and in 42% and 5% of CCL patients. The treatment and prognosis of these patients is described. Radiotherapy was administered in all Stage I and II patients. The probability of survival among patients with localized CBL decreased rapidly during the 12 mo after diagnosis. In contrast, only three patients with CCL exhibiting Stage II disease died during the follow-up period. Stage III and IV patients primarily received chemotherapy. Stage III and IV CBL patients showed a more rapid decrease in probability of survival during the 12 mo following diagnosis than did CCL patients. After yr 1, differences in survival between advanced CTL and CBL patients disappeared. A comparable difference was found between advanced CCL and CTL during yr 2 of follow-up. These findings suggested that patients with advanced CTL occupy an intermediate position between typical low-grade and typical high-grade malignant non-Hodgkin's lymphoma. (22 Refs)

16. CLINICAL AND PROGNOSTIC HETEROGENEITY OF NON-HODGKIN'S LYMPHOMAS OF HIGH-GRADE MALIGNANCY.

Schmalhorst U, Bartels H, Boll I, Burger-Schuller A, Common H, Fulle HH, Graubner M, Heinz R, Huhn D, Leopold H, Meusers P, Nowicki L, Nurnberger R, Oertel J, Ruhl U, Sieber G, Schmidt M, Schoengen A, Strassner A, Schwarze E W, Brittinger G
Div. Haematology, Dept. Medicine, Univ. Essen, Hufelandstrasse 55, D-4300 Essen, W. Germany
Blut; 43(3):201-211 1981

Clinical data and disease development of 150 previously untreated non-Hodgkin's lymphoma (NHL) patients (64 CBL: centroblastic; 55 IBL: immunoblastic; and 31 LBL: lymphoblastic) were studied prospectively CBL, IBL, and LBL were compared. More than half of the CBL and IBL patients were greater than 65 yr old; no sex predominance was seen. Among LBL patients, 16/31 were young adults (median age 21.5 yr); elderly LBL showed an age distribution similar to that in CBL and IBL. Males predominanted in LBL. Rapid lymph node enlargement within less than 3 mo was noted in 56% of CBL, 62% of IBL, and in 64% of LBL patients. Elevated RBC sedimentation rates were observed in greater than 70% of cases; constitutional (B) symptoms were observed in 42% of CBL, 54% of IBL, and 47% of LBL patients. Significant prognostic differences among the three groups were not observed during yr 1 of follow-up. LBL differed in many clinical aspects from CBL and IBL. Extralymphatic organs, primarily bone marrow, were much more frequently affected by LBL (61%); therefore the rate of Stage IV disease increased to 73% in LBL as compared with 28% in CBL and 33% in IBL. There was no initial localized extranodal manifestation in LBL. LBL patients showed an 11-mo median survival time. The prognosis for CBL, IBL, and LBL patients is described. Elderly LBL patients exhibited the worst prognosis. A much better response to radiotherapy and/or chemotherapy was observed for CBL than IBL. The relevance of prognostic differences among these three groups of high-grade malignancies is discussed. (22 Refs)

17. PRINCIPLES AND PRESENT STATUS OF A PROSPECTIVE MULTICENTER STUDY ON THE CLINICAL RELEVANCE OF THE KIEL CLASSIFICATION.

Brittinger G, Schmalhorst U, Bartels H, Fulle HH, Gerhartz H, Gremmel G, Grisar T, Grupp HJ, Gunzer U, Huhn D, Koeppen KM, Kubanek B, Leopold H, Loffler H, Lohr GW, Nowicki L, Ruhl U, Schmidt M, Stacher A, Theml H, Lennert K
Div. Haematology, Dept. Medicine, Univ. Essen, Hufelandstrasse 55, D-4300 Essen, W. Germany
Blut; 43(3):155-166 1981

A prospective study of 814 non-Hodgkin's lymphoma (NHL) patients was conducted. Almost 70% of these patients had lymphomas of low-grade malignancy. Complete data were available for 511/814 NHL patients. Clinical and prognostic data for patients diagnosed according to the Rappaport classification showed that NHL with favorable and unfavorable histologies can be distinguished. NHL with favorable and unfavorable histologies were characterized by a series of features typical for NHL patients of low- (LG) and high-grade (HG) malignancy as defined by the Kiel classification. NHL with favorable histologies and NHL with LG malignancy were predominantly B-cell neoplasias. NHL with unfavorable histologies and NHL of HG malignancy comprised T-, B-, and non-T/non-B-cell neoplasias. The clinical relevance of the Kiel classification in differentiating two major NHL groups was further supported by the higher survival probability of patients with LG malignancy than HG malignancy. (55 Refs)

18. PRIMARY BRAIN LYMPHOMAS. ANATOMOCLINICAL, ULTRASTRUCTURAL AND IMMUNOCYTOCHEMICAL STUDY ABOUT 23 CASES.

Hassoun J, Andrac L, Gambarelli D, Toga M
Laboratoire d'Anatomic Pathologique et de Neuropathologie, 27, Boulevard Jean Moulin, F 13385 Marseille Cedex 5, France
Ann Pathol; 1(3):193-203 1981

Twenty-three cases of primary brain lymphomas were morphologically studied. Electron microscopy was done in 12 cases and immunoperoxidase reactions for light chains of Ig in 10 cases. The patients were 14 males and 9 females. Except two children, the mean age was 50 yr. Clinical features and pre-operative investigations lacked any specificity. Post-operative radiotherapy could be performed in 13 patients, 11 of them being still alive with a follow-up varying from 2.5 mo to 4.5 yr. All the other patients pursued fulminating course (max: 4.5 mo). Tumors were preferentially located in frontal and temporal lobes. On gross examination, well limited tumors were more frequent than ill-defined or purely infiltrating tumors. Microscopically, all the lymphomas were of the diffuse type. Perivascular clusters of lymphoma cells, meningeal and parenchymal infiltrates and sub-ependymal sprouts were found in the peritumoral areas. The lymphomas were cytologically characterized according to the modified Kiel classification using light and electron microscopic data. Thirteen lymphoblastic lymphomas (with 1 convoluted-cell type), 1 centroblastic lymphoma, 8 immunoblastic lymphomas (2 with plasmacytic differentiation) were identified. Light chains of human Ig were immunocytologically demonstrated in 6 of 12 tumors tested, all the positive cases corresponding to immunoblastic lymphomas. A unique case of primary meningeal Hodgkin's disease was found. These results were compared with the rare previous reports associating these different morphological investigations. (Author abstract) (26 Refs) (In FRE)

19. MALIGNANT LYMPHOMA IN THE NOSE: CLINICOPATHOLOGICAL DIFFERENCES FROM THE MALIGNANT HISTIOCYTOSIS PRESENTING AS LETHAL MIDLINE GRANULOMA.

Aozasa K, Ikeda H, Masaki N, Watanabe Y
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Pathol Res Pract; 172(1/2):161-169 1981

The clinical records and histologic materials from seven cases with malignant lymphoma (ML) in the nose were examined, and the results were compared to those in malignant histiocytosis (MH) presenting as lethal midline granuloma previously reported by us. The main differences in the clinical findings were (1) younger initiation of the disease in MH than in ML (mean values were 56 and 37 yr of age, respectively); (2) ML showed a polypoid nasal mass with necrosis but MH showed necrotic granulomatous lesions; and (3) much better survival in ML than in MH. The histological findings of malignant lymphoma differed from malignant histiocytosis not only in monotony but also in cytologic details. Alpha-naphthyl acetate and butyrate esterase reactions gave clear distinction between the two diseases. From these findings, we conclude that malignant lymphoma should be clinicopathologically separated from malignant histiocytosis. (Author abstract) (17 Refs)

20. THE ASSOCIATION OF LYMPH NODES SCINTIGRAPHY WITH 99TCM-SULFUR-MICROCOLLOID AND SONOGRAPHY SCAN IN STAGE DIAGNOSIS OF LYMPHOMAS.

Giubbini R, Bettini R, Casucci R, Garancini S, Magistretti G, Roncari G
Servizio di Medicina Nucleare, Spedali Civili, 25100 Brescia, Italy
Radiol Med (Torino); 67(11):823-827 1981

Thirty-seven patients (16 with Hodgkin's disease, 21 with non-Hodgkin's disease) were studied using indirect scintigraphy (IS) with 99Tcm-sulfur-microcolloid and sonography to evaluate the diagnostic sensitivity of the two methods. IS demonstrated a high sensitivity and a low specificity and was clinically valuable if negative. S had a low sensitivity and a high specificity and was clinically valuable if positive. Sensitivity, specificity and accuracy results for IS were 88%, 80% and 81%, and for S were 59%, 100%, and 81%, respectively. Both methods, especially if associated, were useful in restaging after therapy, where parameters included low risk and stress for the patients, easy execution and low costs. (11 Refs) (In ITA)

21. UPTAKE OF THYMIDINE IN LYMPHOMA CELLS OBTAINED THROUGH FINE-NEEDLE ASPIRATION BIOPSY. RELATION TO PROGNOSIS IN NON-HODGKIN'S LYMPHOMAS.

Brandt L, Olsson H, Monti M
Dept. Oncology, Univ. Hosp., S-221 85 Lund, Sweden
Eur J Cancer Clin Oncol; 17(11):1229-1233 1981

In vitro uptake of tritiated thymidine was studied in autoradiographic preparations of lymphoma cell suspensions obtained through fine-needle aspiration biopsy from 28 patients with non-Hodgkin's lymphoma. The labeling indices (LI) were highest in patients with histiocytic or poorly differentiated lymphocytic lymphoma. during a 2-yr period there was a significant correlation between LI and survival, ie, high LI were associated with a poor prognosis. The results indicate that, in addition to morphology, estimation of the proliferative activity of lymphoma cells may be of clinical significance. (Author abstract) (9 Refs)

22. SERUM SULFHYDRYL CONCENTRATIONS IN PATIENTS WITH MALIGNANT LYMPHOMA.

Grimaldi MG, Caprio G
2nd Dept. Medicine, Fatebenefratelli Hosp., Corso di Porta Nuova 23, 20121 Milano, Italia
Tumori; 67(5):411-413 1981

The total concentration of protein sulfhydryl (SH) groups was determined in the sera of 15 patients with untreated malignant lymphoma (4 patients with Hodgkin's disease and 11 with non-Hodgkin's malignant lymphoma) using 5,5'-dithiobis (2-nitrobenzoic acid) (DTNB). Serum SH total concentration in all patients was markedly depressed and significantly lower than that observed in the sera of healthy controls matched for sex and age. (Author abstract) (12 Refs)

MALIGNANT LYMPHOMA: CHEMOTHERAPY

23. NON-HODGKIN'S LYMPHOMA IN CHILDREN: RESULTS OF TREATMENT WITH THE MODIFIED LSA2-L2 PROTOCOL.

Vecchi V, Pession A, Serra L, Rosito P, Mancini AF, Paolucci G
Section Pediatric Hematology/Oncology, Dept. Pediatrics, St. Orsola Hosp., Massarenti, 11, 40138 Bologna, Italy
Med Pediatr Oncol; 9(5):483-491 1981

From June 1976 to May 1980, 25 previously untreated children with non-Hodgkin's lymphoma (NHL) were studied and treated with a protocol modified from the one (LSA2L2) proposed by Wollner. Stage III and IV had, in addition, prophylactic treatment of the CNS with cranial irradiation (2,400 rad plus intrathecal methotrexate). The complete remission rate is 96%. Of these patients, 76% are disease free surviving after a median observation time of nearly 2 yr. The disease-free actuarial survival is 100% for 6 children with Stage I-II disease and 68% for 19 Stage III-IV children after median observation times respectively of 25+ and 19+ mo. None of the 19 high-risk patients developed CNS disease after prophylactic treatment. Mediastinal involvement and leukemic conversion at diagnosis were not unfavorable prognostic factors, but primary skeletal or sc disease and Burkitt-type histology were ominous features in patients treated by this regimen. It is concluded that good results are obtained when an aggressive multimodal and multiple drug regimen like the LSA2-L2 is coupled with CNS prophylaxis and is used assiduously to maintain complete remission during the first 12 mo of treatment. (Author abstract) (19 Refs)

24. ADRIAMYCIN, BLEOMYCIN, VINBLASTINE AND DTIC IN ADVANCED DIFFUSE LYMPHOCYTIC POORLY DIFFERENTIATED LYMPHOMA.

Grigoletto E, Tirelli U, Tumolo S, Galligioni E, Veronesi A, Trovo MG, Franchin G, De Paoli A, Volpe R, Carbone A
Div. Radiotherapy and Medical Oncology, Ospedale Civile, 33170 Pordenone, Italia
Tumori; 67(5):477-481 1981

From January 1975 to December 1979, 14 consecutive patients with advanced (Stage III-IV) diffuse lymphocytic, poorly differentiated lymphoma (DLPD) were treated with adriamycin, bleomycin, vinblastine and DTIC (5-(3,3-dimethyl-1-triazeno)-imidazole-4-carboxamide) (ABVD). Either maintenance combination chemotherapy with CVP or radiotherapy over bulky disease was added in the cases with complete response (CR). Fifty per cent of the patients achieved CR and 80% achieved objective responses. Among CRs, 100% were alive at 2 yr, 70% of them without evidence of disease. Overall, 75% of the patients were alive at 2 yr, 30% without evidence of disease. Toxicity was acceptable and no drug-related deaths occurred. ABVD is not the ideal combination for DLPD, but it should be taken into consideration in patients with advanced DLPD in which first line combination chemotherapy regimens are not successful. (Author abstract) (21 Refs)

25. CONTINUOUS 5-DAY INFUSION OF VINDESINE IN THE TREATMENT OF LEUKEMIAS AND LYMPHOMAS.

Maraninchi D, Gastaut JA, Tubiana N, Carcassonne Y
Clinique des Maladies du Sang, Institut F. Paoli-I, Calmettes, 232, Boulevard de Sainte-Marguerite, F-13273 Marseille Cedex 9, France
Bull Cancer (Paris); 68(4):338-342 1981

Vindesine is a semisynthetic vinca alkaloid. The short plasma half-life suggested that continuous infusion can improve the therapeutic results by maintaining a constant plasma level. Twenty one patients (acute lymphoblastic leukemia = 5 cases; blastic crisis of chronic myelocytic leukemia = 6 cases; lymphomas = 10 cases) received 5-day vindesine infusion (0,7 mg/m2/d). All these patients had previously several treatments and were resistant to usual chemotherapies including other vinca alkaloids (76% of cases). Eighteen patient were evaluable for response: 13 (72%) had partial responses or minor regressions. Toxicity was not important. Continuous 5-day infusion of Vindesine might be used widely in patients with blood diseases. (Author abstract) (16 Refs) (In FRE)

26. TWO POLYCHEMOTHERAPY REGIMENS IN GENERALIZED NON-HODGKIN'S LYMPHOMA CLASSIFIED ACCORDING TO THE KIEL CLASSIFICATION. A RETROSPECTIVE ANALYSIS.

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Afdelingen for onkologi og radioterapi, Odense sygehus, DK-5000 Odense C, Denmark
Ugeskr Laeger; 143(42):2740-2744 1981

Sixty-one patients with non-Hodgkin's lymphoma (NHL) classified according to Kiel, were treated with two different polychemotherapy regimens in nonrandomized groups. Group I, including 34 patients (11 patients in Stage III and 23 in Stage IV; 12 patients with NHL of low-grade malignancy, 17 with NHL of high-grade malignancy, and 5 unclassifiable patients) was treated according to the MOPP protocol consisting of nitrogen mustard (9 mg iv on days 1 and 8), vincristine (VCR: 2 mg iv on days 1 and 8), procarbazine (150 mg/day po on days 1-14), and prednisolone (PR: 60 mg/day po on days 1-14), repeated 6 times at monthly intervals. Group II, including 27 patients (6 in Stage III and 21 in IV; 13 with low-grade malignancy, 9 with high-grade malignancy, and 5 unclassifiable patients), was treated according to the VEPA protocol consisting of VCR (2 mg iv on day 1), cyclophosphamide (600 mg iv on day 1), adriamycin (60 mg iv on day 1), and PR (100 mg/day po on days 1-5) repeated 6x at monthly intervals, then one course was given every other mo for 6 mo, then one course every 3 mo for 1 yr. The median age was 64 yr in both groups. The complete remission (CR) rate was 17/34 in Group I and 15/27 in Group II. The partial remission rate was 11/34 in Group I and 7/27 in Group II. Six patients in Group I and five in Group II did not respond to the therapy. Permanent remission (in 30% of the cases) was achieved only in Group II patients with NHL of high-grade malignancy. The length of remission and survival was also longer in Group II than in Group I, and the VEPA regimen p roved to be less toxic than MOPP. (15 Refs) (In DAN)

27. VM 26 IN ADVANCED MYCOSIS FUNGOIDES.

Tirelli U, Carbone A, Tumolo S, Galligioni E, Veronesi A, Trovo MG, Grigoletto E
Div. Radiotherapy and Medical Oncology, Ospedale Civile, 33170 Pordenone, Italia
Tumori; 67(5):487-490 1981

Five consecutive patients with progressive extracutaneous Stage IV mycosis fungoides (MF) were treated with VM 26, 100 mg/m2 iv, for at least 3 cycles. All patients had been extensively pretreated and in particular with vinca alkaloids. Two partial responses of 5 and 9+ mo duration and 1 minimal response of 5 mo duration were obtained. Transient myelosuppression was encountered in all patients. These preliminary results should encourage further exploration of VM 26, even in less advanced MF. (Author abstract) (6 Refs)

MALIGNANT LYMPHOMA: RADIOTHERAPY

28. TOTAL-BODY IRRADIATION IN ADVANCED NON-HODGKIN'S LYMPHOMA.

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Inst. Cancer Res., Royal Marsden Hosp., Downs Road, Sutton, Surrey, England

Br J Radiol; 54(646):878-881 1981

Thirty-seven patients with advanced non-Hodgkin's lymphoma who were treated by total-body irradiation (TBI) at the Royal Marsden Hospital are reviewed. Twenty-four patients had received no previous therapy; 13 patients were in relapse. The overall response rate was 73% for nodular lymphomas and 80% for those with diffuse disease. The duration of complete response ranged from two to 41 mo (median 12 mo). Subsequent chemotherapy was given successfully except in patients with prolonged thrombocytopenia which appeared to be related to an initially involved bone marrow. Hemibody irradiation (HBI) was the least myelosuppressive form of TBI and is now being used in complete remission following chemotherapy. (Author abstract) (8 Refs)

MALIGNANT LYMPHOMA: SELECTED PRE-CLINICAL STUDIES

29. ANTIGENIC CHANGES OF A MURINE LYMPHOMA BY IN VIVO TREATMENT WITH TRIAZENE DERIVATIVES.

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Inst. Pharmacology, Univ. Perugia, Via del Giochetto, 06100 Perugia, Italy

Cancer Immunol Immunother; 11(4):283-286 1981

The capacities of five aryltriazenes to produce drug-mediated increases in tumor immunogenicity (DMITI) in murine lymphoma were examined. L1210Ha leukemias were maintained over a number of transplant generations in male and female C57BL/6(H-2b) and (DBA/2Cr x BALB/cCR)F1 (CD2F1) (H-2d/H-2d) mice. Mice were untreated, immunodepressed with cyclophosphamide, or treated with one of the test compounds. The tumor subline used for the test was resistant to the cytotoxic effects of 5-(3,3-dimethyl-1-triazeno)-imidazole-4-carboxamide (DTIC) and the five aryltriazenes. Tumor immunogenicity was substantially increased after four to five transplant generations of treatment with any one of four of the aryltriazenes. The fifth ar yltriazene had no DMITI effect, possibly due to its short half-life. Results indicate that the previously reported DMITI effect of DTIC does not require the presence of the imidazole group, which is present in DTIC but absent from the five compounds tested. The two N3-methyl groups were unnecessary for activity. Cytotoxic activity was not necessary for appearance of immunogenic changes. (11 Refs)

30. IDENTIFICATION OF ANTIGENIC DETERMINANTS UNIQUE TO THE SURFACES OF CELLS TRANSFORMED BY EPSTEIN-BARR VIRUS.

Kintner C, Sugden B
Div. biology, California Inst. Technology, Pasadena, CA, 91125
Nature; 294(5840):458-460 1981

Four monoclonal antibodies (anti-EBVCS) that detect antigenic determinants unique to the surfaces of Epstein-Barr virus (EBV)-transformed cells but are not associated with virus production were isolated. Cell lines transformed in vitro or those transformed in vivo but not associated with Burkitt's lymphoma bound anti-EBVCS strongly, whereas cell lines from patients with Burkitt's lymphoma bound them at intermediate levels or not at all. When untreated lymphocytes and lymphocytes exposed to EBV, Concanavalin A, and pokeweed mitogen were assayed, only EBV-exposed lymphocytes expressed EBVCS determinants, which were detectable within 48 hr after infection. Assay of unseparated populations of EBV-exposed primary lymphocytes and immunoglobulin-positive and -negative populations indicated that those cells which express EBVCS determinants are separated as B cells along with those which express the EBV-induced nuclear antigen and that the two antigen-expressing populations are overlapping and may be identical. A polypeptide with an apparent mol wt of 45,000 was precipitated from an EBVCS-positive cell line and was likely to be the molecule which carries EBVCS determinants. The results indicate that EBVCS determinants are expressed at reduced levels on cell lines established from Burkitt's lymphoma patients relative to expression on other EBV-transformed cell lines. EBVCS determinants are among possible determinants recognized by autochthonous, cytotoxic T cells specific for EBV-transformed cells and may therefore be equivalent to lymphocyte determined membrane antigen (LYDMA); this possibility was supported by the finding that EBVCS and LYDMA were expressed with the same time course in lymphocytes infected with EBV in vitro. If the EBVCS determinants are used by cytotoxic T cells to identify their targets, reduced expression of EBVCS on Burkitt's lymphoma cell lines is consistent with these tumor cells having been selected in vivo to survive that cytotoxic response. (18 Refs)

MALIGNANT LYMPHOMA: REVIEWS

31. THE LYMPHOMAS, LYMPHADENOPATHY, AND HISTIOCYTOSES.

Murphy SB
St. Jude Children's Res. Hosp., Memphis, TN
Hematology of Infancy and Childhood Volume II. Nathan DGand Oski FA, ed. Philadelphia, W. B. Saunders Company, 774 pp., 1981.

Epidemiology and incidence, etiology, histopathology, clinical presentations, laboratory findings, staging, treatment, complications, and prognosis of Hodgkin's disease (HD) are reviewed. Non-Hodgkin's lymphoma, (all primary malignancies of lymphoreticular tissue not classified as HD), are discussed separately from HD because of important differences in the neoplastic cells of origin, clinical behavior, and management of the disorder. Pseudolymphomas, non-neoplastic lymphadenopathy, and histiocytic syndromes are presented. (264 Refs)

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
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HE 20. 3173/2:

HODGKIN'S DISEASE: DIAGNOSIS AND STAGING

1. THE PRETREATMENT PERIPHERAL BLOOD LYMPHOCYTE COUNT IN 1100 PATIENTS WITH HODGKIN'S DISEASE: THE PROGNOSTIC SIGNIFICANCE AND THE RELATIONSHIP TO THE PRESENCE OF SYSTEMIC SYMPTOMS.

MacLennan KA, Vaughan Hudson B, Jelliffe AM, Haybittle JL, Vaughan Hudson G
(c/o G. Vaughan Hudson) Dept. Oncology, Middlesex Hosp., London W1, England
Clin Oncol; 7(4):333-339 1981

The pretreatment peripheral blood lymphocyte count was determined in 1,100 patients who entered the British National Lymphoma Investigation of Hodgkin's disease. The lymphocyte count was found to be normal in only 52.7% of patient at presentation. An abnormal lymphocyte count adversely affected the prognosis. There was a direct inverse relationship between the lymphocyte count and the occurrence of systemic symptoms. These effects were most marked for histologies other than nodular sclerosing Hodgkin's disease. (Author abstract) (13 Refs)

2. LYMPHOGRAPHIC STUDIES ON THE GROWTH DYNAMICS OF PRIMARY MALIGNANT LYMPHOMA.

Morenz R, Kunze ML, Roder K
Medizinische Universitatsklinik der KMU, Johannisallee 32, DDR-7010 Leipzig, E. Germany
Radiol Diagn (Berl); 22(4):452-456 1981

Lymphographic study of the growth dynamics of primary malignant lymph node neoplasia in 112 patients is reported. Hodgkin's disease was diagnosed in 74 cases, reticulosarcoma in 30, lymphosarcoma in 5, Brill-Symmers syndrome in 2, and chronic lymphocytic leukemia in 1. The mean tumor doubling time (MTDT) was 51.5 days in the women and 59.4 days in the men with Hodgkin's disease, and 64.8 days in the women and 79.9 days in the men with reticulosarcoma. Except for lymphosarcoma, where the iliac lymph nodes showed no growth, the lumbar lymph nodes slow growth, and the inguinal lymph nodes rapid growth, there were no preferred lymph node groups with especially slow or rapid growth in the 106 patients. The range of the MTDT values were higher and their ranges wider in the patients with primary lymph node neoplasias than the corresponding parameters of metastases of primary organ tumors, which were determined in control patients. Predilection of both the primary lymph node neoplasias and of lymph node metastases of primary organ tumors for the left lumbar node group was confirmed. (no Refs) (In GER)

3. HISTOLOGICAL TYPE AND LYMPHOGRAPHIC PICTURE IN HODGKIN'S DISEASE.

Bujar H
Dept. Roentgenology 06, 'C. Devila' Hosp., Calea Grivitei 4, Bucharest, Romania
Radiol Diagn (Berl); 22(4):449-451 1981

The histological type and dominant lymphographic aspect of lymph nodes were compared in 106 patients with Hodgkin's disease (HD), and their relationship with survival was analyzed. Lymphocyte predominance (LP) was found in 20 cases, nodular sclerosis (NS) in 12, mixed cellularity (MC) in 30, and lymphocyte depletion (LD) in 44. Dominant lacunar aspect of lymph nodes was found in 69 cases (in 18/20 patients with LP, in 6/12 with NS, in 27/30 with MC, and in 18/44 with LD), reticular-macular aspect in 20 (in 2/20 patients with LP, in 3/12 with NS, in 2/30 with MC, and in 13/44 with LD), and lymph drainage obstruc tion in 17 cases (in 3 patients with NS, in 1 with MC, and in 13 with LD). The mean survival time was longest for the patients with lymph drainage obstruction, but the mean interval between lymphography and death was also shortest in this group. The interval between the onset of the first clinical symptom and lymphography was longest in this group. The mean survival was shortest in the group of patients with dominant reticular-macular lymph nodes. (no Refs) (In GER)

HODGKIN'S DISEASE: CLINICAL IMMUNOLOGY AND IMMUNOTHERAPY

4. THE IN VITRO EFFECT OF A CALF THYMUS EXTRACT (THYMOSTIMULIN) ON THE IMMUNOLOGIC PARAMETERS OF PATIENTS WITH UNTREATED HODGKIN'S DISEASE.

Martelli MF, Velardi A, Rambotti P, Cernetti C, Bracaglia AM, Ballatori E, Davis S
(c/o Davis) Oncology/Clinical Hematology, Veterans Admin. Medical Center, East Orange, NJ, 07019
Cancer; 49(2):245-250 1982

The in vitro effect of a calf thymus extract, thymostimulin (TP-1), on the E-rosette-forming capacity and on the PHA blastogenic response of peripheral blood lymphocytes was evaluated in 20 patients with untreated Hodgkin's disease. The mean percentage of lymphocytes forming E rosettes increased in patients from 44.2% to 57.5% (p less than 0.005). The mean PHA stimulation index rose with all three concentrations tested, but returned to the normal range only with the highest PHA concentration (60 u/ml). An increase in the immune parameters was greatest in those patients who presented with decreased E-rosetting cells or total lymphocyte counts or whose disease was Stage III or IV or of mixed cellular histology. (Author abstract) (30 Refs)

HODGKIN'S DISEASE: SURGERY

5. THROMBOTIC RISKS OF STAGING LAPAROTOMY WITH SPLENECTOMY IN HODGKIN'S DISEASE.

Dawson AA, Bennett B, Jones PF, Munro A
(c/o Bennett) Dept. Medicine, Aberdeen Royal Infirmary, Foresterhill, Aberdeen AB9 2ZB, Scotland
Br J Surg; 68(12):842-845 1981

No significant excess of deep vein thrombosis (DVT) as measured by the 125I-labelled fibrinogen method was observed in patients having staging laparotomy and splenectomy for Hodgkin's disease (HD) compared with patients having elective cholecystectomy under highly standardized surgical conditions. Patients who did have DVT all had splenic involvement with HD. There was no correlation between the post-splenectomy thrombocytosis and the occurrence of DVT. Patients with non-Hodgkin's lymphoma (NHL) and splenomegaly had a high incidence of DVT after splenectomy. (Author abstract) (19 Refs)

HODGKIN'S DISEASE: MULTIMODAL THERAPY

6. 14. A SOUTHWEST ONCOLOGY GROUP: CHEMOTHERAPY VERSUS CHEMOTHERAPY PLUS RADIOTHERAPY IN TREATMENT OF STAGE III HODGKIN'S DISEASE.

Grozea PN, De Persio EJ, Coltman CA, Fabian CJ, Morrison FS, Gehan EA, Jones SE

Oklahoma Medical Res. Foundation, Dept. Medicine, Univ. Oklahoma, Coll. Medicine , 825 N.E. 13th St., Oklahoma City, OK, 73104

Recent Results Cancer Res; 80:83-91 1982

The Southwest Oncology Group (SWOG) performed a randomized study (SWOG 7518, CAR 2) of chemotherapy using 10 courses of nitrogen mustard, vincristine, procarbazine, and prednisone (MOPP) plus low-dose bleomycin (LDB), versus three courses of combined therapy, MOPP + LDB plus radiotherapy (XRT) from October, 1974, to April 1980, in pathologic Stage III Hodgkin's disease. The present report includes data on 136 registered patients, of whom 112 are fully or partially evaluable. At this preliminary analysis, complete remission rates are 82% for chemotherapy alone and 82% for combined treatment. There are no statistically significant differences in survival or relapse-free survival between the two treatment programs, and no specific trends for Stage IIIA versus IIIB. The estimated 3-yr survival rate for all patients was 82%. Toxicities are comparable when considering the highest grades. There was one case of acute myeloblastic leukemia on combined treatment. Preliminary evidence suggests that patients with nodular sclerosis histologic type are more likely to relapse on chemotherapy alone than on combined therapy. (Author abstract) (14 Refs)

7. CHEMOTHERAPY-RADIOTHERAPY VERSUS CHEMOTHERAPY IN HODGKIN'S DISEASE WITH BONE MARROW INVOLVEMENT: RETROSPECTIVE ANALYSIS OF 32 CASES.

Andrieu JM, Cramer P, Asselain B, Tea N, Tricot G, Flandrin G, Jacquillat C, Bernard J

Institut de Recherche sur les Leucemies et les Maladies du Sang, Hopital Saint-Louis, 2, place du Dr. A. Fournier, F-75010 Paris, France

Acta Haematol (Basel); 66(4):217-225 1981

A retrospective analysis was performed on 32 patients suffering from Hodgkin's disease with bone marrow involvement treated between 1972 and 1976. After six courses of chemotherapy (MOPP for 25 patients), we observed 20 complete remissions (62.5%), 8 lymph node partial remissions (bone marrow sterilization but persistence of pathological lymph nodes) and 4 failures. Among the 28 complete or partial responders, 17 received maintenance chemotherapy alone, 9 were submitted to 40 Gy and 2 to 20 Gy irradiations. Fifteen patients died and 8 relapses occurred - all in previously involved lymph node areas. Survival of complete and partial responders is significantly different (p = 0.01) according to whether they received maintenance chemotherapy alone (34.5%) or irradiation (75.7%). Disease-free duration is also significantly different (p = 0.05) according to whether the patients received maintenance chemotherapy alone (42.1%) or 40 Gy irradiation (100%). (Author abstract) (22 Refs)

8. BONE INVOLVEMENT IN HODGKIN'S DISEASE.

Newcomer LN, Silverstein MB, Cadman EC, Farber LR, Bertino JR, Prosnitz LR

Dept. Medicine, Yale Sch. Medicine, 333 Cedar St., New Haven, CT, 06510

Cancer; 49(2):338-342 1982

Eighteen patients with osseous involvement were identified from a series of 124 consecutive patients treated with combined-modality therapy with advanced-stage or relapsing Hodgkin's disease. Multiple lesions were seen as frequently as were solitary lesions. Nodular sclerosing histology was as prevalent as mixed cellularity disease. However, those five cases initially diagnosed at protocol entry were predominantly mixed cellularity (80%) with multiple lesions (80%). Sites of involvement included: the spine, 24; pelvis, 8; ribs, 4; femur, 3; skull, 1; and shoulder 1. Actuarial survival for these patients was 84% at 9 yr. Only three patients were induction failures and no patient has had a relapse. Patients with bone lesions had favorable responses to combined-modality therapy. (Author abstract) (23 Refs)

HODGKIN'S DISEASE: CASE REPORTS

9. MANAGEMENT OF THE PREGNANT PATIENT WITH HODGKIN'S DISEASE.

Jacobs C, Donaldson SS, Rosenberg SA, Kaplan HS
Dept. Medicine, Stanford Univ. Sch. Medicine, Stanford, CA
Ann Intern Med; 95(6):669-675 1981

Fifteen pregnant women with Hodgkin's disease were followed. Five patients had irradiation, 1,000 to 3,000 rad to the neck, mediastinum, or both, during the second or third trimester with normal outcome of pregnancy. One patient had a spontaneous abortion in the first trimester after radiotherapy of 4,400 rad to the breast, an estimated fetal dose of 9 rad. One patient who received chlorambucil throughout pregnancy delivered a normal infant. Six patients had therapeutic abortions; one had early induction of labor. In one patient previously treated for supradiaphragmatic Hodgkin's disease, detection of a subdiaphragmatic relapse was delayed because of pregnancy. We recommend abortion for patients who develop Hodgkin's disease early in pregnancy or who have received chemotherapy or irradiation during the first trimester. During the latter half of pregnancy, asymptomatic disease may be closely followed but early delivery is recommended. Supradiaphragmatic, symptomatic disease can be treated with modified irradiation. For subdiaphragmatic, symptomatic, or extranodal disease, single-agent chemotherapy may be preferable. Treatment requires individualization to insure that the patient will be cured and the fetus protected. (Author abstract) (39 Refs)

10. COEXISTENCE OF A PRIMARY IMMUNODEFICIENCY DISORDER AND HODGKIN'S DISEASE: EVIDENCE AGAINST A B-LYMPHOCYTE ORIGIN FOR THE REED-STERNBERG CELL.

Bobrove AM, Onder O, Myers TJ, Rickles FR, Pastuszak WT, Martin RS, Hild DH
Palo Alto Medical Clinic, 300 Homer Ave., Palo Alto, CA, 94301
Cancer; 48(12):2624-2629 1981

A 44-yr-old woman with a life-long history of recurrent sinopulmonary infections developed Hodgkin's disease with characteristic Reed-Sternberg cells in a biopsy specimen of a mediastinal lymph node. Hypogammaglobulinemia was documented on several serum determinations and plasma cells were absent from biopsy specimens of the lymph node and bone marrow. Immunochemical studies failed to demonstrate any B lymphocytes bearing surface immunoglobulin or Fc-receptors for IgG in the peripheral blood. Pokeweed mitogen stimulation of the patient's peripheral blood lymphocytes in vitro resulted in the development of virtually no plasma cells. Peripheral blood T-lymphocyte number and function were defective initially. Following chemotherapy and radiotherapy, peripheral blood E-rosette-forming cells returned to normal, but T-cell function remained defective and B lymphocytes remained undetectable. These findings are compatible with the presence of two separate immune disorders: a primary hypogammaglobulinemia and Hodgkin's disease. The absence of lymphocytes bearing surface Ig or Fc-receptors for IgG in this patient adds further support against a B-lymphocyte origin for the Reed-Sternberg cell. (Author abstract) (32 Refs)

11. BORDETELLA BRONCHISEPTICA INFECTION IN STAGE IV HODGKIN'S DISEASE.

Stoll DB, Murphey SA, Ballas SK
Cardeza Foundation for Hematologic Res., Philadelphia, PA
Postgrad Med J; 57(673):723-724 1981

It is well known that patients with lymphoproliferative disorders have an altered immune status and are susceptible to opportunistic and non-opportunistic infections. The authors report the first case of a patient with advanced Hodgkin's disease who developed pneumonia caused by the animal pathogen Bordetella bronchiseptica. The most likely source of this organism was the patient's dog. While B bronchiseptica is often responsible for outbreaks of pneumonia and septicemia in wild and domestic animals, its role and incidence in human infections is not known. It is felt that patients with underlying lymphoproliferative diseases and pneumonia should be questioned about any contact with animals. (Author abstract) (8 Refs)

MALIGNANT LYMPHOMA: DIAGNOSIS AND STAGING

12. DIFFERENTIAL DIAGNOSTIC PROBLEMS IN THE RADIOLOGIC EVALUATION OF HISTIOCYTIC LYMPHOMA.

Burgener FA, Hamlin LJ
Dept. Diagnostic Radiology, Strong Memorial Hosp., Box 648, Rochester, NY, 14642
Cancer; 48(12):2589-2595 1981

Medical records, pathologic records, and radiologic examinations of 112 patients with histiocytic lymphoma (HL) were reviewed. Peripheral lymph node enlargement was initially present in less than 50%, while HL presented as localized intraabdominal or intrathoracic lesions in 29% and 13%, respectively. Diagnostic problems encountered during the radiologic evaluation of patients with HL included the following: (1) Localized intraabdominal and intrathoracic lesions could mimic a variety of diseases, most often carcinoma. (2) Intercurrent (opportunistic) infections, which were commonly found in the lungs, and more rarely in the distal esophagus and bone, could easily be mistaken for HL manifestations. (3) Cytotoxic drugs and/or steroids produced pulmonary infiltrates, gastric ulcers, and collapsed vertebral bodies were often indistinguishable from an HL manifestation. (4) A second malignancy, found in 10% of patients either before or after HL was diagnosed, was difficult to differentiate from HL. (5) Aspiration biopsy of localized intraabdominal or intrathoracic HL under fluoroscopic control was unreliable in establishing the correct diagnosis. (Author abstract) (18 Refs)

13. THE ROLE OF ABDOMINAL COMPUTER TOMOGRAPHY IN LYMPHOMA FOLLOWING TREATMENT.

Blackledge G, Mamtora H, Crowther D, Isherwood I, Best JJ
CRC Dept. Medical Oncology, Manchester Univ. and Christie Hosp. and Holt Radium Inst., Wilmslow Road, Manchester M20 9BX, England
Br J Radiol; 54(647):955-960 1981

Two hundred and six patients with biopsy-proven lymphoma, 74 with Hodgkin's disease and 132 with non-Hodgkin's lymphoma had abdominal computed tomography for assessment of remission status (108 patients) or for investigation of relapse (98 patients). In 43 patients with diffuse large cell lymphomas scanned at a time of apparent complete remission CT was abnormal in 21. Sixteen of these patients have relapsed and died. Only one patient has relapsed in the group who have normal CT scans. This difference was significant ($p = 0.00001$). This difference was not seen in nodular lymphomas. There were very few patients with Hodgkin's disease in whom the CT scan was abnormal and there is a suggestion that many abnormalities following treatment may represent inactive Hodgkin's disease or fibrosis only. CT played a major role in diagnosing the full extent of relapse in both non-Hodgkin's lymphoma and Hodgkin's disease. Over 50% of the abnormal sites detected by CT would not have been shown by any other non-invasive investigation. Five patients with treated Hodgkin's disease who had 'B' symptoms only suggesting relapse were all shown by CT to have extensive intra-abdominal disease. (Author abstract) (20 Refs)

14. CORRELATION BETWEEN LYMPHOGRAPHIC PICTURE AND SURVIVAL TIME IN HODGKIN'S DISEASE AND NON-HODGKIN'S LYMPHOMA.

Wiljasalo S
Dept. Roentgenology, Univ. Central Hosp., 70210 Kuopio 21, Finland
Radiol Diagn (Berl); 22(4):447-448 1981

Nine different patterns of the lymphographic picture were distinguished in 168 patients with Hodgkin's disease and non-Hodgkin's lymphoma. The 10-yr follow-up of the patients demonstrated the prognostic significance of the different lymphographic patterns; the closer the lymphographic findings were to normal, the better was the prognosis. The lymphographic picture was found to be able to change in the course of the disease, especially in Hodgkin's disease. (no Refs) (In GER)

15. COMPARISON OF RESULTS OF ULTRASOUND TOMOGRAPHY AND LYMPHOGRAPHY.

Schilling H, Schuller M
Institut fur Rontgendiagnostik (Charite), Schumannstrasse 20/21, DDR-1040 Berlin, E. Germany
Radiol Diagn (Berl); 22(4):493-494 1981

Results of 754 ultrasound tomograms (UST) and 500 lymphograms (LS) for determination of retroperitoneal lymphoma were compared. Agreement between the two methods was 85%. Accuracy was 91% for LG and 93% for UST. LG provided more fine-structural detail of lymph nodes; UST was able to detect liver metastases. The value of UST was confirmed for staging and monitoring of lymph node tumors. (no Refs) (In GER)

16. THYMIC GALLIUM-67 LOCALIZATION IN PEDIATRIC PATIENTS ON CHEMOTHERAPY: CONCISE COMMUNICATION.

Donahue DM, Leonard JC, Basmadjian GP, Nitschke RM, Hinkle GH, Ice RD, Wilson DA, Tunell WP
(c/o Basmadjian)Coll. Pharmacy, Univ. Oklahoma, Oklahoma City Campus, Oklahoma City, OK, 73190
J Nucl Med; 22(12):1043-1048 1981

Localization of Ga-67 in the thymus has been reported to occur in children. In our control group of 87 patients, 15% of children under 5 yr and 11% of children over 5 yr demonstrated thymic localization. In contrast, in our study group of seven children with acute lymphocytic leukemia or malignant lymphoma, lymphocytic diffuse, treated on a modified non-Hodgkin's lymphoma protocol, Sloan-Kettering LSA2-L2 thymic localization occurred during treatment in five of the seven. We conclude that increased thymic gallium localization in children under chemotherapy for a known malignancy may reflect increased activity of thymic medullary epithelial cells and regeneration of thymic lymphocytes during recovery from involution induced by certain chemotherapeutic agents. (Author abstract) (24 Refs)

17. DNA CONTENT AND KINETIC CHARACTERISTICS OF NON-HODGKIN'S LYMPHOMA: DETERMINED BY FLOW CYTOMETRY AND AUTORADIOGRAPHY.

Costa A, Mazzini G, Del Bino G, Silvestrini R
(c/o Silvestrini) Div. Experimental Oncology, Instituto Nazionale per lo Studio e la Cura dei Tumori, Via Venezian 1, 20133 Milan, Italy
Cytometry; 2(3):185-188 1981

Samples of malignant lymph nodes obtained from 74 non-Hodgkin's lymphoma (NHL) patients were cultured; DNA content and 3H-thymidine labeling index (LI) were determined. Propidium iodide was the DNA-specific fluorescence dye used in cytofluorography. Ploidy was expressed as the ratio of relative DNA content of human lymphoid G0/1 cells to that of chicken red blood cells. Of the NHL, 45/74 (61%) were aneuploid, and 91% of those showed a hyperdiploid DNA content. The max frequency of aneuploid tumors (72%) in comparison to diploid tumors (28%) was found in the group with unfavorable histology (original Rappaport classification), but the observation was not significant. Tumors with high proliferative activity showed a significantly (p less than 0.01) lower percentage of cells in G0/1 and a higher percentage of cells in S (P less than 0.01) than those with low proliferative activity. An analysis of 21 cases with a homogenous cell population indicated that the S phase fractions, as determined by cytofluorometry and autoradiographic LI, are correlated (r = 0.95, p less than 0.01). (19 Refs)

18. THE INFLUENCE OF HISTOLOGIC TYPE ON THE INCIDENCE AND DURATION OF RESPONSE IN NON-HODGKIN'S LYMPHOMA.

Herrmann R, Barcos M, Stutzman L, Walsh D, Freeman A, Sokal J, Henderson ES
(c/o Barcos) Dept. Pathology, Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY, 14263
Cancer; 49(2):314-322 1982

A group of 227 cases of non-Hodgkin's lymphoma included 7 favorable and 4 unfavorable histologic classes with collective median survival times of 83 and 16 mo, respectively. The favorable group included three follicular subgroups (cleaved, mixed, and large noncleaved) and four diffuse classes (small lymphocytic, cleaved, Burkitt's noncleaved, and convoluted lymphocytic). The unfavorable group consisted of four diffuse subgroups (plasmacytoid lymphocytic, mixed, and small and large noncleaved). There were significant differences in collective median survivals between patients in Stage I-II and those in Stage III-IV in both the favorable group (not reached, NR vs 62 mo, p less than 0.001) and the unfavorable group (57 mo vs 12 mo, p less than 0.01). The incidence of complete response to primary treatment was higher in the favorable then in the unfavorable group (75% vs 56%, p = 0.002) and in those with limited as compared with advanced disease. Complete responders in both prognostic groups had longer survival times than did partial or minimal responders. A significant difference in median complete remission duration was found between responders in Stage I-II vs Stages III-IV in the favorable group (not reached vs 40 mo, p = 0.001) but not in the unfavorable one (56 mo vs 22 mo, p greater than 0.05). The absence of relapses after 41 mo among complete responders in the favorable but not in the unfavorable group suggests a potential for cure in a proportion of cases from the former group. The incidence of complete response was lower and median remission duration was shorter after secondary as compared with primary treatment. The results of this study confirm the prognostic value of the Lukes and Collins classification system and the importance of initial staging and of achieving a complete response to primary treatment in both the favorable and unfavorable lymphomas. (Author abstract) (53 Refs)

MALIGNANT LYMPHOMA: CLINICAL IMMUNOLOGY AND IMMUNOTHERAPY

19. IMMUNOCOMPETENCE AND MALIGNANT LYMPHOMA: IMMUNOLOGIC STATUS BEFORE THERAPY.

Anderson TC, Jones SE, Soehnlen BJ, Moon TE, Griffith K, Stanley P
Section Hematology Oncology, Dept. Internal Medicine, Univ. Arizona Coll. Medici ne, Tucson, Arizona, 85724
Cancer; 48(12):2702-2709 1981

One-hundred-eighty-six previously untreated patients with malignant lymphoma were evaluated for immunocompetence by means of several tests of immune function: total circulating lymphocytes, T cells (E-rosettes), B cells (EAC-rosettes), delayed hypersensitivity to six recall antigens, serum immunoglobulins, mixed lymphocyte culture, and lymphocyte mitogenic response to phytohemagglutinin and pokeweed mitogen. The results were correlated with histology, stage, and clinical features. Diffuse lymphomas, especially diffuse histiocytic (large cell) (DHL), were associated with decreased absolute lymphocytes and E-rosette forming cells. Skin test reactivity varied with both histology and stage. For example, only one of six tests was impaired in diffuse lymphocytic well differentiated (DLWD) lymphoma in contrast to two of six in localized DHL and five of six in advanced DHL. Patients with nodular lymphoma exhibited depressed mean levels of IgA and IgG, while only IgA was significantly decreased in diffuse lymphoma. Mitogen stimulation was depressed in all groups, although mixed lymphocyte cultures did not differ significantly from controls. In summary, there is a spectrum of immunodeficiency of both B and T cell type in patients with malignant lymphoma that correlates with histology and stage. Implications and possible mechanisms of these observations are discussed. (Author abstract) (25 Refs)

20. 15. MAINTENANCE IMMUNOTHERAPY WITH BCG IN NON-HODGKIN'S MALIGNANT LYMPHOMAS: A PROGRESS REPORT OF A RANDOMIZED TRIAL.

Hoerni B, Durand M, Eghbali H, Hoerni-Simon G, Richaud P, De Mascarel A

Fondation Bergonie, 180 rue de Saint-Genes, F-33076 Bordeaux Cedex, France

Recent Results Cancer Res; 80:92-97 1982

Ninety-eight patients with non-Hodgkin's malignant lymphoma were first put into complete remission by a combination of chemotherapy and radiotherapy, and then received one course of chemotherapy as reinforcement. They were then randomized to receive either maintenance BCG therapy or no other treatment. Ninety-three patients were available for this analysis. There was a significant difference (p = 0.021) in relapse-free survival times between the two groups of patients. This difference is particularly significant in male patients, in patients ages 50-65 yr, in all histologic classes, in patients treated after an initial relapse, and in clinical Stages I and II . There was also a difference in crude survival, but the difference was not significant. (Author abstract) (7 Refs)

MALIGNANT LYMPHOMA: CHEMOTHERAPY

21. COMBINATIONS OF METHOTREXATE (COP OR CHOP) IN THE TREATMENT OF PREVIOUSLY UNTREATED AND TREATED LYMPHOMAS.

Gomez GA, Stutzman L, Moayeri H, Shimaoka K, Plager J, Han T, Naeher C, Henderson E

Dept. Medical Oncology, Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY, 1 4263

Cancer Treat Rep; 66(1):43-47 1982

A regimen consisting of two courses of methotrexate (MTX) with leucovorin rescue followed 1 wk later by cyclophosphamide, vincristine, and prednisone (MTX-COP) was studied in 10 patients with disseminated diffuse non-Hodgkin's lymphoma who had had no prior chemotherapy. A similar regimen with the addition of doxorubicin (MTX-CHOP) was used for patients who had had previous chemotherapy: 11 with diffuse non-Hodgkin's lymphoma and two with Hodgkin's disease. The response rate to initial MTX administration was 55%, and the clinical onset of effect was usually observed within 48 hr. Responses were observed in previously treated and untreated patients. The remission rate was 100% with both regimens. There were seven complete remissions with MTX-COP and six with MTX-CHOP. The median durations of remission were 23 and 13 mo, respectively; median survival was not reached in each group. MTX was well-tolerated by both groups of patients without serious toxic effects. Overall, significantly more hematologic toxicity was observed in previously treated patients; however, no life-threatening toxic effects were observed in either group. The incorporation of MTX and other antimetabolites into schedules of chemotherapy for previously treated and untreated patients with non-Hodgkin's lymphoma is well tolerated and deserves further exploration. (Author abstract) (11 Refs)

22. COMPARISON OF THE USE OF TENIPOSIDE AND VINCRISTINE IN COMBINATION CHEMOTHERAPY FOR NON-HODGKIN'S LYMPHOMA.

Australian and New Zealand Lymphoma Co-operative Chemotherapy Study Group, Cooper IA, Ding JD, Gunz FW, Vincent PC, Hermann RP, Matthews JR, Probert JC, Stephens EJ, Penington DG, Burns WI, Pitney WR, Sage RE, Dale B, Matthews JP, Motteram R, Crowley K, Palmer AA
(c/o Cooper), Cancer Inst., 481 Little Lonsdale St., Melbourne 3000, Victoria, Australia
Cancer Treat Rep; 66(1):49-55 1982

A total of 164 patients with non-Hodgkin's lymphoma (NHL) were randomized to receive cycles of treatment every 3 wk with either CTP, ie, cyclophosphamide (400 mg/m2/day orally x 5), teniposide (VM-26) (100 mg/m2 iv x 1), and prednisolone (60 mg/m2/day orally x 5), or COP, ie, vincristine (1.4 mg/m2 iv x 1; maximum, 2 mg) with the same cyclophosphamide and prednisolone doses listed above. Results were analyzed according to whether the patients' NHL histology was favorable (47 patients) or unfavorable (117). The great majority of patients in each group had advanced disease (Stage IV in 70% and Stage III in 20%). For each histologic group, the results with the two regimens were similar with respect to remission incidence and survival. In favorable-histology NHL, CTP produced 57% complete remissions (CR) and 29% partial remissions (PR), compared with 54% CR and 19% PR for COP. Survival in these patients was also similar for the two regimens, the relative death rates being 1.13 for CTP-treated patients and 0.88 for COP-treated patients (p = 0.75). In patients with unfavorable-histology NHL, CTP produced 38% CR and 28% PR, compared with 43% CR and 35% PR for COP, the relative death rates being 1.10 for CTP-treated patients and 0.90 for COP-treated patients (p = 0.49). Neurotoxicity was virtually absent in patients treated with CTP, whereas in COP-treated patients it was severe in 12% and moderate in 36%. Other toxic effects occurred with equivalent frequency in the two regimens. These results show that teniposide can replace vincristine in combination with cyclophosphamide and prednisolone in the treatment of NHL, with freedom from neurotoxicity and comparable survival and response rates. (Author abstract) (19 Refs)

23. VP-16-213 IN THE TREATMENT OF STAGE III AND IV DIFFUSE LYMPHOCYTIC LYMPHOMA OF THE LARGE CELL (HISTIOCYTIC) VARIETY: A INTERIM REPORT.

Jacobs P, King HS, Cassidy F, Dent DM, Harrison T
Dept. Hematology, Univ. Cape Town Medical Sch., Res. Center, Anzio Road, Observatory 7925, Cape Town, South Africa
Cancer Treat Rep; 65(11/12):987-993 1981

A pilot study has previously demonstrated antitumor activity for the epipodophyllotoxin VP-16-213 in patients with diffuse lymphocytic lymphoma of the large cell (histiocytic) variety. To define this observation further, a prospective randomized trial was undertaken in patients with Stage III and IV disease, comparing this agent used alone (Group 1, 41 patients) to the response obtained when the same schedule of VP-16-213 was combined with either cyclophosphamide (Group 2, 36 patients) or doxorubicin (Group 3, 41 patients). The quantity of VP-16-213 given to patients in the three groups was equivalent. Of these 118 patients, 3 were lost to followup and thus were excluded from further study. Specifically included were 12 patients who died within 1 mo of diagnosis while still receiving induction chemotherapy. For the three groups, complete remission rates were 39%, 26%, and 54%, and additional partial remissions were obtained in 20%, 11%, and 10% of the patients, respectively. The lower remission rates obtained in patients receiving cyclophosphamide combined with VP-16-213 are statistically significant (p less than 0.05), but no explanation for this is evident since the distribution of poor prognostic factors among the three groups was uniform. The higher percent of complete remission and the greater number of patients remaining free from disease in Group 3 demonstrate the superiority of the combination of VP-16-213 with the anthracycline antibiotic doxorubicin. (Author abstract) (19 Refs)

24. ADRIAMYCIN IN THE TREATMENT OF NON-HODGKIN'S LYMPHOMA.

Parlier Y, Gorin NC, Stachowiak J, Najman A, Duhamel G

Service des maladies du sang, Hopital Saint-Antoine, 184, rue du Faubourg Saint- Antoine, 75571 Paris Cedex 12, France

Sem Hop Paris; 57(41/42):1685-1690 1981

The effectiveness of polychemotherapy including adriamycin (ADR) was studied in 131 patients (61 men and 70 women, 16-81 yr old, median age 57 yr) with non-Hodgkin's lymphoma. One hundred and twelve patients were not pretreated. Lymphocytic lymphoma (LL) was diagnosed in 107 patients and histiocytic lymphoma (HL) in 24. Twenty-two Stage I-II patients with LL, 31 with Stage III-IV nodular LL, 20 with Stage III-IV diffuse LL, and 12 with HL were treated with the combination cyclophosphamide, vincristine and prednisone (CVP). Ten patients with Stage III-IV nodular LL, 24 with Stage III-IV diffuse LL and 12 with HL received additionally ADR (CVP+A). All Stage I-II patients with LL also received radiotherapy. The 1-and 5-yr survival rates equaled 89% for the Stage I-II patients with LL. For the Stage III-IV patients with nodular LL, the 5-yr survival rate was 69% after CVP treatment, vs a 3-yr survival rate of 54% after CVP+A treatment. In the subgroup of Stage III-IV patients with diffuse LL, the complete remission rates were 25% for CVP and 67% for CVP+A, but no significant difference was found in the median survival time. For the patients with HL, the complete remission rates were 50% for CVP and 83% for CVP+A, but the median survival was only 17 mo after CVP treatment, and the 3-yr survival rate after CVP+A treatment was 90%. The findings indicate that CVP is effective in the treatment of nodular LL, but that the addition of ADR is useful in the case of HL. (19 Refs) (In FRE)

25. SPECIAL SYMPOSIUM ON DERMATOLOGICAL THERAPY: III. PSORIASIS AND MYCOSIS FUNGOIDES. RAZOXANE.

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Clin Exp Dermatol; 6(6):647-650 1981

Use of razoxane in the treatment of psoriasis and mycosis fungoides has been examined. Razoxane, a cytostatic bis-dioxopiperazine, arrests cell cycle progression only during premitotic (G2) and early mitotic (M) phases of the cell cycle. The drug inhibits a wide range of tumors, is well tolerated, and is not hepatotoxic. Treatment results in normalization of tumor microvasculature, which is likely responsible for the antimetastatic activity. For these reasons razoxane has also been useful in treatment of psoriasis. (12 Refs)

26. COMBINATION CHEMOTHERAPY WITH CYCLOPHOSPHAMIDE, VINCRISTINE, AND PREDNISONE (CVP) IN TNM-CLASSIFIED STAGE IV MYCOSIS FUNGOIDES.

Tirelli U, Carbone A, Veronesi A, Galligioni E, Trovo MG, Tumolo S, Grigoletto E

Div. Radiotherapy and Medical Oncology, Ospedale Civile of Pordenone, Pordenone 33170, Italy

Cancer Treat Rep; 66(1):167-169 1982

Nine patients with Stage IV mycosis fungoides (MF), according to TNM classification, were treated with cyclophosphamide, vincristine, and prednisone (CVP). CVP induced a 66% overall o bjective response rate and a 44% complete response rate, which is the highest reported in the literature. CVP is an effective regimen in MF and could be employed in combination with total skin or total lymphoid radiotherapy. TNM classification should be used for all patients with MF, because it makes the evaluation and comparison of treatments more reliable. (Author abstract) (15 Refs)

27. SPECIAL SYMPOSIUM ON DERMATOLOGICAL THERAPY: III. PSORIASIS AND MYCOSIS FUNGOIDES. PHOTOCHEMOTHERAPY IN THE TREATMENT OF PSORIASIS AND MYCOSIS FUNGOIDES.

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Dept. Dermatology, Royal Devon and Exeter Hosp., Exeter, Devon, England

Clin Exp Dermatol; 6(6):651-657 1981

Clinical studies in 73 patients with Stage O-III mycosis fungoides have shown that photochemotherapy (PUVA), using methoxsalen and long-wave UV light, induces clinical and histologic remission in Stages O-II and in Stage III when combined with radiotherapy. PUVA usually does not cause tumor regression in Stage III disease. PUVA has a high degree of efficacy in the treatment of psoriasis. Possible long-term hazard of PUVA-associated skin cancer remains to be demonstrated. Studies of other compounds and various PUVA regimens may lead to safer forms of treatment. Guidelines for safe use of PUVA are presented. (20 Refs)

MALIGNANT LYMPHOMA: RADIOTHERAPY

28. SURVIVAL OF PATIENTS WITH LOCALIZED DIFFUSE HISTIOCYTIC LYMPHOMA.

Sweet DL, Kinzie J, Gaeke ME, Golomb HM, Ferguson DL, Ultmann JE

Univ. Chicago, Box 420, 950 East 59th St., Chicago, IL, 60637

Blood; 58(6):1218-1223 1981

Twenty-eight patients with previously untreated diffuse histiocytic lymphoma (DHL) were identified to be in pathologic Stage (PS) I (11), IE (3), II (8), or IIE (6) by exploratory laparotomy and splenectomy. Six patients were treated with total nodal radiotherapy; 14 with an extended mantle; 5 with an inverted Y or whole abdomen; and 3 with an involved field. Twenty-six patients achieved a complete remission (93%) and 2 patients had persistent local disease. The median survival and disease-free survival for the complete response group are 56 and 51.5 mo, respectively. Ten of the 11 Stage I or IE patients had supradiaphragmatic lymph node disease. Patients with Stage I or IE disease (n = 14) demonstrated a median survival of 72.5 mo and a median disease-free survival of 69.5 mo; there

was one disease-related death. Patients with Stage II or IIE disease (n = 14) demonstrated a median survival of 33 mo and median disease-free survival of 29.5 mo; there were 10 relapses or deaths. Patients in Stages I, IE, II, or IIE with infradiaphragmatic disease (n = 7) had a median survival of 36 mo, while patients with supradiaphragmatic presentation (n = 21) demonstrated median survival of 68 mo (p = 0.37). The data indicate that patients with diffus e histiocytic lymphoma with Stage I supradiaphragmatic lymph node disease are curable using radiotherapy alone, achieving a 93% 11-yr actuarial disease-free survival. Patients with Stage II or IIE disease are not readily curable with radiation therapy alone, achieving a 33% 11-yr actuarial disease-free survival; radiotherapy with adjuvant chemotherapy or chemotherapy alone should be considered for this group. (Author abstract) (14 Refs)

29. NON-HODGKIN'S LYMPHOMA PRESENTING AS THYROID ENLARGEMENT.

Chak LY, Hoppe RT, Burke JS, Kaplan HS
Dept. Radiology, Div. Radiation Therapy, Stanford Univ., Stanford, CA, 94305
Cancer; 48(12):2712-2716 1981

From 1969 to 1978, 11 patients with non-Hodgkin's lymphoma presenting as thyroid enlargement were evaluated and treated in the Division of Radiation Therapy at Stanford University Hospital. All patients were staged with lymphangiogram and bone marrow biopsy. Eight patients had Stage I-II disease and three patients had Stage III-IV disease. The histologic pattern of the biopsies were diffuse in nine cases, and eight cases were classified as histiocytic lymphoma. All eight patients with Stage I or II disease were treated with irradiation. There is an 83.3% survival at 3 years and a 75% relapse-free survival at 2 years. No instance of local recurrence was observed in this group of patients. The three patients with Stage III or IV disease were treated by either irradiation or chemotherapy. Two relapsed within 1 year and died with disease; the third remained free of disease for 9 years before relapse and died with disease 6 months later. High dose regional irradiation is the recommended treatment for patients with Stage I-II lymphoma of the thyroid. (Author abstract) (22 Refs)

MALIGNANT LYMPHOMA: MULTIMODAL THERAPY

30. LYMPHOMAS OF THE TESTIS - RESULTS OF TREATMENT 1960-77.

Read G
Dept. Radiotherapy, Christie Hosp., Holt Radium Inst., Manchester, England
Clin Radiol; 32(6):687-692 1981

Fifty-one patients with malignant lymphoma presenting in the testis are reported. The tumors were all diffuse non-Hodgkin's lymphoma. Eight patients had bilateral involvement. Fifty-three per cent of patients had evidence of spread beyond the testis at presentation and 75% at some time. The actuarial survival for all patients was 20% and for patients with disease apparently confined to the testis 40%. There was a survival advantage for patients with right sided tumors and lymphocytic histology. Chemotherapy using the VAP regime followed by radiotherapy to sites of bulky disease is recommended for patients with evidence of spread at presentation. For patients with disease apparently confined to the testis it is suggested that consideration should be given to adjuvant chemotherapy following radiotherapy to the abdominal nodes and scrotum. (Author abstract) (11 Refs)

MALIGNANT LYMPHOMA: CASE REPORTS

31. MONOCLONAL IMMUNOGLOBULINS WITH AFFINITY FOR PLATELETS AND THEIR RELATIONSHIPS TO MALIGNANT LYMPHOMA.

Veenhoven WA, Thomas-van der Schans GS, Nieweg HO
Div. Hematology, Dept. Medicine, Univ. Groningen, P. O. Box 30, 001, 9700 RB Groningen, The Netherlands
Cancer; 49(1):40-42 1982

Monoclonal immunoglobulins with affinity for platelets were detected in the blood of seven patients. Two of these had thrombocytopenia and non-Hodgkin's lymphoma (NHL). One patient had thrombocytopenia and possibly incipient NHL. The other four patients had pseudothrombocytopenia at the time of diagnosis but one of them developed NHL 6 years later. It is suggested that these monoclonal immunoglobulins may in some cases be associated with malignant lymphoma and that subjects presenting with these immunoglobulins should have a long term follow-up in order to elucidate the question whether or not lymphoma will develop. (Author abstract) (18 Refs)

32. NODULAR MIXED CELL LYMPHOMA WITH MONOCLONAL GAMMOPATHY.

Bain GO, Belch A
Cross Cancer Inst., 11560 University Ave., Edmonton, Alberta T6G 1Z2, Canada
Am J Clin Pathol; 76(6):832-837 1981

Malignant lymphomas are rarely accompanied by a serum M component. Such neoplasms are usually of lymphocytic cell type and, with extremely rare exceptions, of diffuse pattern. A patient with an unusual malignant lymphoma of mixed cell type characterized by follicular structures and vascular proliferation was found to have a serum monoclonal gammopathy (IgM kappa) of over 4 g/dl. Remission accompanied by a pronounced reduction in the M protein was achieved with Chlorambucil. Subsequent relapse was characterized by the emergence of a large cell lymphoma with IgM kappa surface immunoglobulin. No concomitant rise in the serum M component accompanied relapse. (Author abstract) (18 Refs)

MALIGNANT LYMPHOMA: SELECTED REPORTS ON ETIOLOGY AND EPIDEMIOLOGY

33. SUPRADIAPHRAGMATIC PRESENTATION OF NON-HODGKIN'S LYMPHOMA IN MEN OCCUPATIONALLY EXPOSED TO ORGANIC SOLVENTS.

Olsson H, Brandt L
Dept. Oncology, Univ. Hosp., Lund, Sweden
Acta Med Scand; 210(5):415-418 1981

Using a standardized interview schedule, occupational exposure to organic solvents was investigated in 61 consecutive male patients with the diagnosis of non-Hodgkin's lymphoma. When exposure was defined as handling of organic solvents every working day for at least 1 yr, 23 patients were exposed and 38 non-exposed. Of 15 patients with clinical Stage I-II above the diaphragm, 12 (80%) were occupationally exposed to organic solvents. Only one (11%) of eight patients with clinical Stage I-II disease located below the diaphragm was exposed. Thirty-seven patients had clinical Stage III-IV disease at the time of diagnosis and 10 (27%) of these were exposed. The predominance of exposed patients in the group with Stage I-II disease above the diaphragm is significant and the results indicate a relation between exposure to organic solvents and supradiaphragmatic presentation of non-Hodgkin's lymphoma. No correlation was found between exposure and the morphology of the lymphomas. (Author abstract) (13 Refs)

34. EPIDEMIOLOGY OF LYMPHOID MALIGNANCY. AN ETIOLOGICAL HYPOTHESIS OF ADULT T-CELL LEUKEMIA/LYMPHOMA.

Tajima K, Tominaga S
Dept. Epidemiology, Aichi Cancer Center Res. Inst., Chikusa-ku, Nagoya 464, Japan
Gan To Kagaku Ryoho; 8(7):1009-1016 1981

In order to study adult T-cell leukemia/lymphoma (ATLL), which is prevalent in Kyushu, an etiological hypothesis of ATLL is proposed. ATLL is found in limited zones in Kyushu, mainly in rural and coastal areas, which are warm in winter and humid in summer. The geographical distribution of filariasis which accompanies several lymphoreticular ailments and was prevalent until 20 yr ago, was found to be closely correlated with that of patients with ATLL. It was also suggested from analysis of the chronological changes in the av wt and height of school children by prefecture that the nutritional condition of the inhabitants of Kyushu might have been poorer than that of other districts, especially in the past. In these respects, it is conceivable that repeated exposure to filarial infection in association with undernourishment and some other factors might have played an important role in the etiology of ATLL. (30 Refs) (In JPN)

MALIGNANT LYMPHOMA: SELECTED PRE-CLINICAL STUDIES

35. IN VITRO GROWTH OF LYMPHOMA COLONIES FROM CHILDREN WITH NON-HODGKIN'S LYMPHOMA.

Smith SD, Wood GW, Fried P, Lowman JT
Dept. Pediatrics, Univ. Kansas Medical Center, Kansas City, KS, 66103
Cancer; 48(12):2612-2623 1981

Growth in vitro of malignant lymphoid cells has been previously reported, but those studies involved direct establishment of cell lines from the patients' cells. In the present study, an in vitro system for both primary growth and passage of malignant lymphoblastic colony-forming cells (ML-CFC) was established, and for the first time, colony-forming cells from non-Hodgkin's lymphoma patients were cultured, and cell lines were established from individual colonies. Malignant lymphoid colonies grew from 9 of 16 (56%) bone marrow aspirates, which were histologically involved with lymphoma and from 5 of 29 (17%) morphologically normal bone marrow samples. ML-CFCs grew concomitantly with myeloid and monocytic CFCs and were distinguishable by their morphologic characteristics on agar, cytochemical staining characteristics, and cell surface markers. Successful passage of ML-CFCs was accomplished in five patients, and 10 distinct cell lines (6 null cell, 3 B cell, and 1 T cell) were established. This agar assay system provides an opportunity to study malignant lymphoma cell growth both as a primary colony and as a cell line established from a primary colony. (Author abstract) (44 Refs)

36. ADRIAMYCIN DAMAGE: IN VIVO REPAIR BY LYMPHOMA CELLS.

Potmesil M, Levin M, Goldfeder A, Silber R
Dept. Radiology and New York Univ. Cancer Center, New York Univ. Medical Sch., 550 First Ave., New York, NY, 10016
JNCI; 67(6):1259-1263 1981

The in vivo repair of ADR-induced cell damage was investigated in the DBA3 transplantable mouse lymphoma. After a single injection of 5 or 15 mg ADR/kg body wt into DBA/2J mice, the survival fraction of clonogens showed a 2.2-to 4.4-fold decrease at 12 or 18 hr post injection and returned to pretreatment levels within 6 hr. These changes were accompanied by the appearance and disappearance of DNA crosslinks and breaks. Because cell division and/or cell loss could not explain the return of clonogens to pretreatment level, the results strongly suggested repair of ADR damage in tumor cells in situ. Such an efficient repair mechanism, responding to a high toxic dose of ADR, constitutes a therapeutically unfavorable event that may contribute to drug resistance. (Author abstract) (27 Refs)

37. IMMUNOSUPPRESSION ASSOCIATED WITH SJL/J MURINE LYMPHOMA. I. SUPPRESSION OF CELL-MEDIATED IMMUNE RESPONSES AFTER TUMOR TRANSPLANTATION.

Kumar RK, Lykke AW, Penny R
Sch. Pathology, Univ. New South Wales, P.O. Box 1, Kensington, New South Wales 2033, Australia
JNCI; 67(6):1269-1275 1981

The proliferative responses of peripheral blood lymphocytes of inbred SJL/J mice to the mitogens phytohemagglutinin and concanavalin A were evaluated serially in individual animals before and after induction of lymphomas by transplantation. Tumor-bearing mice exhibited marked suppression of mitogen responsiveness. Proliferative responses in mixed lymphocyte-tumor cell culture and mixed lymphocyte culture were also suppressed. Suppression of responses was tumor related, and responsiveness was restored in animals whose tumors regressed. There was no deficiency of responder T-cells in the peripheral blood of tumor-bearing animals, and suppressor cell activity was not demonstrable in a number of in vitro assays. However plasma from tumor-bearing animals exhibited potent immunosuppressive activity. The presence of plasma suppressive activity was similarly tumor related. Thus this study demonstrates nonspecific suppression of cell-mediated immune responses following tumor induction, apparently mediated by a plasma suppressor factor. (Author abstract) (35 Refs)

38. IMMUNOSUPPRESSION ASSOCIATED WITH SJL/J MURINE LYMPHOMA. II. CHARACTERIZATION OF A PLASMA SUPPRESSOR FACTOR IN TUMOR-BEARING MICE.

Kumar RK, Lykke AW, Penny R

Sch. Pathology, Univ. New South Wales, P.O. Box 1, Kensington, New South Wales 2033, Australia

JNCI; 67(6):1277-1282 1981

The properties of a factor responsible for immunosuppressive activity in the plasma of inbred SJL/J mice bearing transplanted lymphomas were investigated. Suppressive activity was not due to an intact virus but resided in a soluble molecule characterized as a nonimmunoglobulin protein of mol wt 68,000-88,000. The plasma suppressor factor was relatively stable and was neither directly cytotoxic nor complement-dependent. The degree of suppression of in vitro lymphocyte proliferative responses depended on the time of addition of plasma to cultures. Suppression was reversible if cells exposed to plasma were washed before mitogen stimulation, but stimulated cells exposed to the suppressor factor were irreversibly inhibited. The suppressor factor was partially species-specific. Supernatants from short-term cultures of tumor cells from lymph nodes of SJL/J mice contained a similar suppressor factor, indicating that the plasma factor was probably a product of tumor cells. (Author abstract) (33 Refs)

39. GENE AMPLIFICATION IN METHOTREXATE-RESISTANT MOUSE CELLS. I. DNA REARRANGEMENT ACCOMPANIES DIHYDROFOLATE REDUCTASE GENE AMPLIFICATION IN A T-CELL LYMPHOMA.

Tyler-Smith C, Alderson T

Medical Res. Council Mammalian Genome Unit, King's Building, West Mains Road, Edinburgh EH9 3JT, Scotland

J Mol Biol; 153(2):203-218 1981

Mouse EL4 lymphoma cells have been selected in vitro for resistance to methotrexate. Four independently derived resistant cell lines are described. Each has amplified dihydrofolate reductase (DHFR) genes, and overproduces DHFR RNA and DHFR protein. In three of the four cell lines DNA rearrangement has occurred near the ends of the DHFR gene. The rearrangement is different in each case, but always involves only a proportion of the DHFR genes. (Author abstract) (55 Refs)

40. SPONTANEOUS LYMPHOMAS IN SJL/J-(V+) MICE: ECOTROPIC AND DUALTROPIC VIRUS EXPRESSION IN NORMAL AND LYMPHOMATOUS TISSUES.

De Rossi A, D'Andrea E, Colombatti A, Fischinger PJ, Chieco-Bianchi L

(c/o Chieco-Bianchi) Lab. Oncology, Inst. Pathological Anatomy, Univ. Padova, Via Gabelli 61, 35100 Padova, Italy

JNCI; 67(6):1241-1250 1981

Approx 60% of inbred SJL/J-(v+) adult mice having high levels of ecotropic endogenous XC+ virus showed virus activation within the first mo of life, while the others produced virus at comparable levels later on. In an attempt to correlate the time of virus activation with the incidence and latency of lymphomas, the tails of 57 1-and 2-mo-old mice were tested for virus presence, and the mice were then observed for lymphoma appearance. While all 2-mo-old mice expressed ecotropic virus, only 63% of the 1-mo-old mice were virus-positive. However, no relationship existed between early virus production (within 1 mo) or late virus production and lymphoma latency, total lymphoma incidence, and histopathology. In contrast with high titers of XC+ virus in tail tissues of diseased mice, a markedly low virus content was found in lymphomatous organs. This difference was not due to selective growth of poor virus-producer cells or to inhibitory factors possibly released by the inflammatory cell component. Viral protein content and XC+ virus titer were not closely correlated in the neoplastic organs. Search for XC- viruses revealed that only 1 of 6 aged normal and 16 of 19 lymphomatous mice produced viruses that grew on mink lung cells. By use of a standard limiting dilution cloning procedure, four isolates were obtained that showed tropism for both murine and heterologous cells. Three of these isolates induced cytopathic changes similar to those induced by MCF viruses on mink lung cells but not on mouse cells. Interference and neutralization assays performed to better characterize the virus envelope properties further indicated that SJL/J isolates had features typical of MCF dualtropic viruses. (Author abstract) (67 Refs)

41. INHIBITION OF THE YC8 LYMPHOMA GROWTH BY ALLOIMMUNIZATION WITH NORMAL CELLS.

Parmiani G, Sensi ML, Schirrmacher V, Bortin M, Martin WJ

Div. Experimental Oncology A, Istituto Nazionale Tumori, Via G. Venezian 1, 20133 Milano, Italy

Transplant Proc; 13(4):1906-1909 1981

Effects of alloimmunization with normal mouse lymphoid cells were studied in relation to the resistance of BALB/c mice to the growth of syngeneic Moloney virus-induced lymphoma YC8, previously shown to lack detectable amounts of alien H-2 antigens. Alloimmunization of BALB/c mice with normal lymphoid cells elicited a strong resistance to otherwise lethal doses of YC8 cells; the phenomenon was particularly evident and reproducible in mice immunized either with B10.A, B10.D2, or pool 5 lymphoid cells. Neither H-2 differences nor route of immunization affected the response. Alloimmunization with tissues of a single strain were less effective in reducing the growth of other syngeneic lymphomas and sarcomas. However, pool immunization with tissues of five different strains significantly retarded the growth of the BALB/c radiation-induced lymphoma RL(male)1, and of the urethan-induced BALB/c lymphoma Ur-1. The presence of effectors capable of killing YC8 cells in alloimmune BALB/c mice was examined in vitro. Efficacy of B10.D2 or DBA/2 but not of B10.A immunization in inducing anti-YC8 effectors indicated that in vivo and in vitro systems may have different requirements for the immune response. Immunity to YC8 was restricted by gene products of the major histocompatibility complex, possibly the Kd-IEd regions, in only the in vitro en vironment. The mechanism by which alloimmune prevention operates may involve a cross-reaction between antigens of normal allogeneic lymphocytes and antigens expressed by the tumor, natural killer-like cells, viral antigens, or alloreactivity. (14 Refs)

MALIGNANT LYMPHOMA: REVIEWS

42. BURKITT'S LYMPHOMA.

Ambrus JL, Ambrus CM
Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY, 14263
J Med; 12(6):385-413 1981

Clinical and epidemiologic features of Burkitt's lymphoma are reviewed. Epidemiologic studies suggest that simultaneous infection with Epstein-Barr (E-B) virus and malaria may be involved as etiologic agents. On the other hand we have found that in the Amazon region of Brazil and Peru both malaria and E-B virus infection is common among children, yet Burkitt's lymphoma is rare. The possibility exists that other concomitant etiologic agents and genetic factors are also involved. Several investigators suggested the possible involvement of Reo 3 virus. We have found antibodies against Yaba virus. A laboratory worker who accidentally inoculated himself with Yaba virus developed a histiocytoma which when inoculated into Asiatic monkeys produced typical Yaba tumors. This was the first case that Koch's postulates were fulfilled in a virus induced neoplasm in man. Therapeutically, the best clinical results were obtained in those patients who were treated with small doses of cyclophosphamide. On the basis of somewhat inadequate follow-up studies, it is estimated that '5 year cures' were obtained in about 10% of the patients. (Author abstract) (44 Refs)

43. LYMPHOMA OF THE BREAST.

Schouten JT, Weese JL, Carbone PP
(c/o Weese) Dept. Surgery, Univ. Wisconsin, 600 Highland Ave., Madison, WI, 53792
Ann Surg; 194(6):749-753 1981

Thirteen patients with lymphoma of the breast are presented. In addition, 163 previously reported cases of lymphoma of the breast are reviewed. Complete staging was performed on all patients. No patient had a diagnosis of lymphoma prior to breast biopsy. The histologic findings were diffuse histiocytic lymphoma (DHL) in eight patients, nodular lymphocytic poorly differentiated lymphoma (NLPD) in two patients, nodular mixed lymphoma (NM) in two patients and nodular sclerosing Hodgkin's disease (NSHD) in one patient. Five patients had Stage IV disease, two had Stage III disease, four had Stage II disease and two had Stage I disease. Nine patients each underwent an excisional biopsy and four patients each had a modified radical mastectomy as initial therapy. Two patients each underwent a staging laparotomy. In advanced disease, chemotherapy achieved complete remissions in approximately 50% of patients. Unfavorable histologic findings are most common in lymphoma of the breast and thorough staging is necessary to select the best form of therapy. The absolute survival rate (61%) and the disease free survival rate (46%) are similar to nodal lymphoma of corresponding histologic factors and stage. (Author abstract) (18 Refs)

44. LYMPHOMAS INVOLVING THE GASTROINTESTINAL TRACT.

Gray GM, Rosenberg SA, Cooper AD, Gregory PB, Stein DT, Herzenberg H
Div. Gastroenterology, Stanford Univ. Medical Center, Stanford, CA, 94305
Gastroenterology; 82(1):143-152 1982

Staging, distribution, and therapy of lymphomas occurring in the gastrointestinal tract are discussed. During examination for staging, special attention should be directed to the lymphoid tissue of Waldeyer's ring (the nasopharynx, tonsils, and base of the tongue), since this is a site of non-Hodgkin's involvement. In addition to the lymphogram for staging, opacified retroperitoneal lymph nodes are valuable indicators for extent of disease, response to therapy, and subsequent relapse. Lymphoma is considered 'primary' in the gastrointestinal tract when initial symptoms are in the abdomen or the disease presents as a disturbance of gastrointestinal function. Occult or unrecognized involvement of the gastrointestinal tract at onset and during the course of disease in patients with widespread lymph node involvement is more common than usually appreciated by clinicians. Histologic subtype of the lymphoma as well as extent or stage of disease are important factors to be considered in therapy. Case reports illustrate diagnostic and therapeutic strategies. (36 Refs)

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
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HE 20.3173/2:

HODGKIN'S DISEASE: DIAGNOSIS AND STAGING

1. IMPORTANCE OF INITIAL MEDIASTINAL ADENOPATHY IN HODGKIN DISEASE.

North LB, Fuller LM, Hagemeister FB, Rodgers RW, Butler JJ, Shullenberger CC
Dept. Diagnostic Radiology, Univ. Texas System Cancer Center, M.D. Anderson Hosp. and Tumor Inst., 6723 Bertner Ave., Houston, TX, 77030
AJR; 138(2):229-235 1982

The importance of initial mediastinal disease was studied retrospectively in 189 patients with Stages I, II, and III Hodgkin disease treated at the M D Anderson Hospital and Tumor Institute between 1969 and 1976. Stages I and II patients with mediastinal disease at presentation had an 88% 5 yr survival rate compared with a 98% survival rate for those without mediastinal disease. Disease-free survival was 66% vs 78%. Stage III patients with and without initial mediastinal disease showed essentially the same 5 yr survival rate (75% vs 78%), but showed a lower disease-free survival of 60% in those with mediastinal disease as compared with 74% in those without mediastinal disease. Because of the prognostic importance of mediastinal disease and its extent at initial presentation, computed tomography is recommended to evaluate patients with low neck or supraclavicular adenopathy in whom there is no obvious mediastinal adenopathy and in all Hodgkin disease patients in whom there is questionable mediastinal disease or suggestion of lung extension on routine radiographs. Treatment plans have been altered to include chemotherapy and low-dose irradiation to the lungs in those patients with mediastinal mass diameters of 7.5 cm or greater, regardless of stage. (Author abstract) (18 Refs)

2. DIAGNOSTIC EVALUATION OF GALLIUM-67 SCANNING OF INTRATHORACICAL NEOPLASMS - CLINICAL AND EXPERIMENTAL RESULTS.

Pabst HW, Kempken K, Langhammer H
Nuklearmedizinische Klinik und Poliklinik, Technischen Universitat Munchen, Ismaninger Str. 22, D-8000 Munchen 80, W. Germany
Int J Nucl Med Biol; 8(4):295-302 1981

One hundred forty two patients suffering from bronchial carcinoma and 118 with Hodgkin's disease were examined scintigraphically by use of 67Ga-citrate. Additionally, in 31 patients with bronchial carcinoma the specific 67Ga concentration was determined in tissue samples of histomorphologically various tumors. One hundred thirty two of 142 (93%) of bronchial carcinomas demonstrated a significantly increased radiogallium accumulation by scintigraphy. No differences between differentiated and undifferentiated tumors could be observed. These clinical-scintigraphical results could be confirmed by direct measurement of 67Ga concentration in tumor tissue. Independent of the histomorphological type 67Ga concentration was found to be 20.3 +-6.7% kg-1 tumor tissue. Normal lung tissue yielded 3.2 +-1.6% kg-1 whereas necrotic tumor tissue containing up to 30% viable tumor cells, revealed 7.9 +-2.4% kg-1 of injected 67Ga. The comparison of x-ray and 67Ga scintigraphy showed concordant results (true-positive/true-negative) within the thorax region in 90.6% of the 84 untreated and in 93.6% of the 34 treated patients suffering from Hodgkin's disease. In the neck and thorax region only 0.5% false-positive and 4.2% false-negative findings were obtained. In untreated patients with one or more Hodgkin's lesions a focally increased 67Ga accumulation was detected in 81.2% but in treated patients only in 27.1%. Therapy resulted in a marked decrease in the number of scintigraphically detectable lymphomas. No significant difference in behavior of 67Ga accumulation could be observed in the various histomorphological types. Gallium-67 imaging is useful for determination of tumor size and extent in bronchial carcinoma as well as in intrathoracically situated Hodgkin's disease prior to therapy. After a tumor specific therapy gallium-67 scintigraphy is suitable for evaluation of the effectiveness of radiation or chemotherapy and for detection of recurrent lymphomas. (Author abstract) (23 Refs)

HODGKIN'S DISEASE: CLINICAL IMMUNOLOGY AND IMMUNOTHERAPY

3. MONOCYTE FUNCTION IN HODGKIN'S DISEASE.

Holm G, Bjorkholm M, Johansson B, Mellstedt H, Lindemalm C
Institutionen for klinisk immunologi, Huddinge sjukhus, 141 86 Huddinge, Sweden
Clin Exp Immunol; 47(1):162-168 1982

Monocyte functions were studied in 16 patients with Hodgkin's disease, 11 untreated and 5 in unmaintained complete remission. Eleven untreated patients with non-Hodgkin's lymphomas and 21 healthy persons were used as controls. Monocytes were isolated from peripheral blood and enriched to greater than 90%. Lymphoma monocytes showed normal ability to lyse human RBC coated with anti-D IgG antibodies as evaluated by a 51Cr-release assay. The ability of monocytes to augment or suppress concanavalin A stimulation of lymphocytes purified to greater than 98% was studied by incubation of a number of lymphocytes with increasing amounts of purified monocytes. The incorporation of 14C-thymidine was potentiated by a factor of 10 in the presence of equal amounts of monocytes. There was no difference between monocytes from Hodgkin, non-Hodgkin or healthy controls to augment patients' autologous or normal lymphocytes. Patient monocytes also suppressed the response at the same monocyte-lymphocyte ratio as normal monocytes. Stimulation of patient lymphocytes without the addition of monocytes was usually lower than that of normal control lymphocytes. The difference between patient and control lymphocyte stimulation was preserved in the presence of monocytes. It is concluded that monocytes from patients with active Hodgkin's disease or non-Hodgkin's lymphoma have normal helper and suppressor effects on patient or normal lymphocytes stimulated by Con A and normal antibody-dependent cytotoxicity. (Author abstract) (31 Refs)

HODGKIN'S DISEASE: CHEMOTHERAPY

4. THE EFFECTS OF HODGKIN'S DISEASE AND COMBINATION CHEMOTHERAPY ON GONADAL FUNCTION IN THE ADULT MALE.

Whitehead E, Shalet SM, Blackledge G, Todd I, Crowther D, Beardwell CG
(c/o Shalet) Dept. Endocrinology, Christie Hosp., Wilmslow Road, Manchester M20 0BX, England
Cancer; 49(3):418-422 1982

The effects of Hodgkin's disease and quadruple chemotherapy on gonadal function have been investigated in 93 male patients with Hodgkin's disease. Nineteen men were studied before they received chemotherapy. Fifteen of the 19 had a sperm count of 20 million/ml or greater and motility was at least 40% in all 15. In the remaining 74 men, gonadal function was studied after completion of chemotherapy (6 mo-8 yr). Semen was obtained from 49 men who had received six or more courses of MVPP. Forty-two were azoospermic and 5 of the remaining 7 had a sperm count below 1 million/ml. Decreased libido and sexual activity was common during treatment but in the majority of men these returned to normal after completion of chemotherapy. The median FSH and LH levels and the median increments in semen FSH and LH levels after LHRH administration were significantly elevated compared with an age-matched control group. The mean testosterone level of the patients was significantly lower than in controls suggesting Leydig cell damage but androgen replacement therapy was not indicated in any individual patient. No evidence of hyperprolactinemia as a result of MVPP therapy was found. These results suggest that sperm storage before chemotherapy represents the main possibility for these patients to have children after completing chemotherapy. Before starting chemotherapy, advice should be given to these patients concerning possible changes in sexual behavior during treatment and the very high incidence of permanent infertility following treatment. (Author abstract) (21 Refs)

5. HODGKIN'S DISEASE: CHEMOTHERAPY.

Golomb HM, Sweet DL
Div. Biologic Sciences, Pritzker Sch. Medicine, Chicago, IL
Curr Ther; 28:296-302 1981

Staging and treatment of Hodgkin's disease (HD) are presented. Treatment of HD by radiation therapy (RT) according to stage of disease is outlined. The standard and best combination chemotherapy for HD patients is MOPP, given every 28 days and consisting of nitrogen mustard, 6 mg/square meter [m2], days 1, 8, iv, oncovin, 1.4 mg/m2 days 1, 8, iv, procarbazine, 100 mg/m2, days 1-14, po, and prednisone, 40 mg/m2, days 1-14, po. Dosage may be modified according to WBC and platelet counts. A 10-yr follow-up of 198 patients treated with MOPP showed that all asymptomatic patients with Stage III or IV disease achieved complete remission. Good results were achieved with the five-drug combination of carmustine, vinblastine, cyclophosphamide, procarbazine, and prednisone. The ABVD combination, doxorubicin, bleomycin, vinblastine, and dacarbazine (DTIC) given every 28 days produces complete remissions as with MOPP and is successful in patients who have failed with MOPP. A modification of ABVD including adriamycin has also been used in patients who fail MOPP. Side effects of the regimens are discussed. The combined use of RT and chemotherapy increases risk of a second cancer 29x compared to 3x for either therapy alone. Re-treatment of relapses after RT is discussed. (no Refs)

6. HODGKIN'S DISEASE AND PREGNANCY.

Klener P, Nemecek K, Donner L
II. Interni klinika, Fakultna nemocnica 1 s poliklinikou KUNZ SKNV, U nemocnice 2, 128 08 Prague 2, Czechoslovakia
Cas Lek Cesk; 120(48):1425-1427 1981

Seven 17-30-yr-old women with Hodgkin's disease became pregnant 2-4 yr after the end of chemotherapy. One patient was initially in Stage IIB, four were in Stage IIIB, and two in IVB. Mixed cellular type was found in five patients, nodular sclerotic type in two. All patients were subjected to chemotherapy. Six patients were treated with the combination chlormethine-vincristine-procarbazine-prednisone, another with vinblastine (VLB), and one patient received additionally chemotherapy with the combination adriblastin-bleomycin-dacarbazine-VLB. Three patients were also irradiated. The pregnancies proceeded without complications and terminated in spontaneous births of healthy babies. Only one baby was premature. Two patients developed recurrences after childbirth, the five others have been in remission for 8 mo to 4 yr. The chemotherapy had no effect on fertility and appeared to have no influence on fetal development or on the stability of the remission from the underlying disease. (15 Refs) (In CZE)

HODGKIN'S DISEASE: RADIOTHERAPY

7. ETIOLOGY OF PERICARDIAL EFFUSION FOLLOWING RADIATION THERAPY OF HODGKIN'S DISEASE.

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Strahlentherapie; 157(9):571-575 1981

Radiation doses delivered to the anterior pericardium between 1969 and 1979 were ascertained in 16 patients with Hodgkin's disease, in whom pericardial effusions had developed after multiple-field therapy using five ventral fixed fields to the mediastinum as a supra-diaphragmatic primary treatment. The appearance of effusions was directly dependent on the dosage, if doses between 53 and 128 Gy had been delivered; in such patients, seriousness of the clinical symptoms was related to the importance of the dose delivered to the anterior pericardium. Control groups consisted of two collectives comprising 9 patients with primary pericardial affection due to Hodgkin's disease, and 11 comparable further patients without complications after mantle treatment; in these collectives, 1 case in the second group excepted, antisarcolemmal antibodies were not observed. On the other hand, these antibodied could be detected in 5 out of 11 patients with Hodgkin's disease who suffered from pericardial complications following radiation therapy. Possible diagnostic and pathogenetic significance of the present findings is discussed. (Author abstract) (18 Refs) (In GER)

8. PREGNANCY IN HODGKIN'S DISEASE PATIENTS.

Baisogolov GD, Shishkin IP, Shchelkonogova LN
Inst. Medical Radiology, Obninsk, USSR
Ter Arkh; 53(11):126-129 1981

Thirty-six women who became pregnant after diagnosis of Hodgkin's disease (HD) are reviewed. Of these patients, 21 had localized HD (Stage I-II), 9 were in Stage III, and 6 were in Stage IV. One patient received polychemotherapy alone, 2 received polychemotherapy together with radiotherapy, and 33 received radiotherapy alone. The patients who were irradiated received distant gamma therapy from two opposite fields (single focal dose 200-220 rads, 5x/wk, total dose 4,000-4,500 rads to the clinically involved lymph nodes and 3,500-4,000 rads to the zones of subclinical metastatic spreading). The patients in Stage I-II received irradiation of the lymph nodes above the diaphragm and of the spleen. The patients in Stages III-IV received irradiation of the supradiaphragmatic lymph nodes, spleen, para-aortal lymph nodes, and subdiaphragmatic lymph nodes. Three patients received treatment during pregnancy (5, 14, and 30 wk of gestation), while 33 became pregnant after the treatment. All patients had normal pregnancy and delivery; follow-up of the children for 2-10 yr showed normal psychomotor development. Eight patients developed recurrences within the first 24 mo after the treatment. (6 Refs) (In RUS)

HODGKIN'S DISEASE: MULTIMODAL THERAPY

9. CYTOGENETIC STUDIES IN PATIENTS PREVIOUSLY TREATED FOR HODGKIN'S DISEASE.

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Cancer Genet Cytogenet; 5(1):25-35 1982

A cytogenetic study was made of bone marrow cells and lymphocytes from patients who had been successfully treated with various regimens for Hodgkin's disease. Most of the patients had been off treatment for at least 3 yr before the study began. They were divided into three groups according to the intensity of the therapy received. The frequency of gaps and breaks in the chromosomes of lymphocytes was above normal limits and similar in the three treatment groups. In contrast, the frequency of both lymphocytes and bone marrow cells with rearranged karyotypes was correlated with the intensity of treatment. Clones of cells with an abnormal karyotype were found in only two patients, both of whom were in the group receiving the most intensive therapy, ie, chemotherapy and total nodal irradiation. (Author abstract) (15 Refs)

10. THE DECISION BETWEEN SINGLE- AND COMBINED-MODALITY THERAPY IN HODGKIN'S DISEASE.

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Am J Med; 72(1):63-70 1981

Using the technique of decision analysis to evaluate data on single-modality and combined-modality therapy in Hodgkin's disease, we have been able to determine which treatment gives the best chance for prolonged disease-free survival in given settings. Both the potential of combined-modality therapy for inducing secondary hematologic malignancies and the rate of salvage with MOPP following relapse after radiotherapy have been studied to observe the effect of different rates of these variables on the therapeutic decision. An analysis of patients with known pathologic stage endorsed the continued use of extended-mantle radiotherapy for Stages IA and IIA disease; under most of the conditions analyzed, combined-modality therapy appeared the best option for Stage IIIA disease. The results for Stages IB and IIB disease showed neither combined-modality therapy nor total nodal irradiation to have a conclusive advantage. We also analyzed management decisions for patients who had not had pathologic staging. For this, probabilities of each pathologic stage were derived from a large patient data base and were incorporated into the decision analysis. The results of this analysis indicated that, despite the mortality of laparotomy, treatment designated according to pathologic stage was more effective than immediate combined-modality therapy for most types of patients. For certain patients in whom the clinical features could be used to predict a high probability of advanced disease, the most effective management was immediate MOPP chemotherapy without staging laparotomy. (Author abstract) (22 Refs)

11. NON-GONADIC COMPLICATIONS OF CHEMORADIOTHERAPY IN HODGKIN'S DISEASE. A STUDY OF EIGHTY-THREE PATIENTS.

Bolla M, Sotto JJ, Barjhoux R, Kolodie H, Vincent F, Michallet M, Sarrazin R, Vrousos C, Hollard D

Service de Radiotherapie, Centre Hospitalier Universitaire de Grenoble, 38700 La Tronche, France

Sem Hop Paris; 58(4):204-208 1982

Eighty-three patients with Hodgkin's disease were treated with a combination of chemotherapy and radiotherapy. Forty-three were included in Protocol 1 (from January 1970 to January 1974) and 40 in Protocol 2 (February 1974 to December 1977). In Protocol 1, staging laparotomy was not systematically performed (20 cases). Treatment consisted of two iv injections of vinblastine and total nodal irradiation. In protocol 2, laparotomy was systematic in patients over 50 (35 cases). Patients with Stages I and II were treated as mentioned above. Patients with Stage III received two Mopp courses followed by total nodal irradiation. Patients older than 50 with Stages I and II and poor prognosis factors received chemotherapy only. Laparotomy was associated with a 0% mortality rate and a 3.6% morbidity rate. No myelitis or pericarditis were observed. Herpes zoster occurred in 24% of the patients, pulmonary apex fibrosis in 6%, hy pothyroiditis in 2.4%, and leukopenia in 3.6%. Two late infectious complications were fatal. No solid tumor was apparent. Acute leukemia and non-Hodgkin malignant lymphoma developed in two patients. Good tolerance, shortness of treatment, and remission rate, warrant the pursuit of Protocol 2 in which systematic laparotomy for patients under 50 allows total nodal irradiation and therefore reduction of chemotherapy. (Author abstract) (23 Refs) (In FRE)

12. HODGKIN'S DISEASE IN CHILDREN: LONG-TERM THERAPEUTIC RESULTS.

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Bull Cancer (Paris); 68(5):456-464 1981

Between 1965 and 1976, 83 previously untreated children aged 15 yr and under, with biopsy-confirmed Hodgkin's disease were assessed, treated, and followed-up at the Hospital Saint-Louis, in Paris. Clinical stages were IA-IIA for 59, IB-IIB for 19, and III-IV for 5 patients. Two main types of treatment were used: monochemotherapy-radiotherapy in 26 patients who received mantle field irradiation followed by monthly vinblastine injections for 3 yr; 57 patients received a combination of MOPP and radiotherapy. The MOPP-radiotherapy treated patients have a significantly better survival and relapse-free survival than the monochemotherapy-radiotherapy treated patients (86.9% vs 76.1% and 83.5% vs 65.4%). Thirteen relapses were observed after a median complete remission period of 30 mo: 6 patients are now free from disease and 1 is still under treatment. Ten patients died after a 55 mo median survival: 7 died from Hodgkin's disease and 3 from treatment toxicity. No secondary cancer or leukemia has been observed. The main long-term complications of therapy were sterility in male patients, after chemotherapy, and growth defects and disturbances of thyroid functions after radiotherapy. (Author abstract) (47 Refs) (In FRE)

MALIGNANT LYMPHOMA: DIAGNOSIS AND STAGING

13. NON-HODGKIN'S LYMPHOMAS. ANALYSIS OF 109 JAPANESE CASES WITH THE USE OF LSGJ CLASSIFICATION.

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Am J Pathol; 106(1):30-39 1982

Recently the Lymphoma Study Group of Japan (LSGJ) proposed a new classification of non-Hodgkin's lymphomas (NHLs), dividing NHLs into the follicular group consisting of three subsets and the diffuse group, 7. Each subset of the diffuse group is further divided into B or T cell types according to immunologic markers and/or morphologic prediction. In the review of 118 malignant lymphomas, the authors studied the 109 cases of NHLs, attempting to assess the clinicopathologic utility of this classification. Morph ologic criteria, enzyme histochemistry, and immunoperoxidase technique were used to ensure the accuracy of the immunologic phenotyping. The results suggest that the LSGJ classification is easily reproducible and yields a more precise clinicopathologic correlation than traditional, morphologic classifications. Consistent with similar studies in Japan, this study demonstrated a low incidence of Hodgkin's disease (7.6% of all lymphomas) and follicular lymphomas (8.3% of all NHLs) and a high incidence of T cell lymphomas (34.9% of all NHLs). The incidence (45.9%) of extranodal presentation was high. These four features seem characteristic of lymphomas in Japan. (Author abstract) (24 Refs)

14. A NEW HISTOLOGICAL CLASSIFICATION OF MALIGNANT LYMPHOMAS (LSG CLASSIFICATION) AND ITS SIGNIFICANCE.

Mikata A, Suchi T, Wakasa A, Kikuchi M, Namba K, Mohri M, Mori S, Tojima K, Watanabe S, Harigoya S, Itagaki T, Matsuda M, Kirino Y, Takagi K, Mikata A
Dept. Pathology, Keio Univ. Sch. Medicine, Tokyo, Japan
Nippon Ketsueki Gakkai Zasshi; 44(7):1401-1410 1981

Findings of the present work further support the rationale of LSG classification in regards to clinical behaviors and therapeutic approaches as well as origin of cells and their functional specificities. As revealed in the present work, large cell type was a heterogenous group and it would be further subdivided in the future. We believe this classification is in value not only in Japan, but in areas where T-cell lymphomas predominate over B-cell tumors. (Author abstract) (24 Refs)

15. NON-HODGKIN'S LYMPHOMA: A CLINICO-PATHOLOGIC STUDY USING A NEW HISTOPATHOLOGICAL CLASSIFICATION.

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Second Dept. Internal Medicine, Aichi Cancer Center Hosp., Nagoya, Japan
Nippon Ketsueki Gakkai Zasshi; 44(7):1411-1419 1981

Clinical features of 359 cases of non-Hodgkin's lymphoma classified by a new method were analyzed. Follicular lymphoma seemed to be a uniform group, and a clear relationship among histologic types was observed. Large cell type constituted the majority of diffuse lymphomas. No obvious difference between the medium-sized cell, mixed and large cell types was observed. Pleomorphic and lymphoblastic types were both peculiar and characteristic subtypes with a very poor prognosis. The results of this study corroborate the usefulness and clinical relevance of the new histopathological classification. Survival advantage was shown to be much more related to the clinical stage within follicular and diffuse lymphoma than the histologic type. Difference in survival was caused by the difference in the distribution of the clinical stage in each histologic type. (Author abstract) (11 Refs)

16. CLINICAL, HEMATOLOGICAL AND PATHOLOGICAL FEATURES OF T-CELL LEUKEMIA-LYMPHOMA IN THE NAGASAKI DISTRICT.

Kinoshita K, Kamihira S, Yamada Y, Amagasaki T, Ikeda S
Dept. Hematology, Atomic Disease Inst., Nagasaki Univ. Sch. Medicine, Nagasaki, Japan
Nippon Ketsueki Gakkai Zasshi; 44(7):1431-1443 1981

Surface natures of malignant cells from lymph nodes and the peripheral blood of 140 patients with non-Hodgkin's lymphoma (NHL) in the Nagasaki district were examined for T and B cell characteristics. Surprisingly, 110 cases (78.6%) were of the T-cell form on the basis of spontaneous rosette formation with sheep erythrocytes. Of the remaining cases, 17 were B-cell origin (monoclonal S-Ig positive), 9 were non T-, non B-cell and 4 cases were undetermined. Seventy-one (65.4%) of the T-cell lymphomas were of leukemic form, characterized by pleomorphism in the peripheral blood cell size, and histological appearance. However, most of the leukemic T-cells showed obvious lymphocytic differentiation, with condensed nuclear chromatin and scant cytoplasm, although in many of the cases, lymphomatous infiltrate was dominated by either pleomorphic lymphoid cells or medium-sized cells, accompanied by occasional large multinucleated lymphoid cells. Clinically, they primarily involved middle-aged and elderly subjects, and were characterized by wide spread organ invasion (particularly to the liver, spleen and skin), susceptibility to various infections, complication of hypercalcemia and a poor prognosis. A mediastinal mass was not observed in all cases. The patients had a median survival of only 7.5 mo. On the other hand, non-leukemic T-cell lymphomas, half of which histologically showed the monotonous infiltrates of large lymphoid cells, were not different in any way from usual manifestation of malignant lymphoma with massive lymphadenopathy. These patients were generally resistant to chemotherapy and many of them died of the progression of the lymphoma within almost 1 yr. On the basis of surface marker, cell morphology, cytochemistry, and DNA synthesis of the malignant, pleomorphic T-cells, it was suggested that large lymphoid cells, namely, T-immunoblast differentiated to mature lymphocytes, resulting in a pleomorphism of the lymphoid infiltrates and leukemic manifestation. (Author abstract) (32 Refs)

17. PREDICTABILITY OF IMMUNOLOGIC PHENOTYPE BY MORPHOLOGIC CRITERIA IN DIFFUSE AGGRESSIVE NON-HODGKIN'S LYMPHOMAS.

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Am J Clin Pathol; 77(1):46-49 1982

Diffuse aggressive non-Hodgkin's lymphomas are immunologically and morphologically heterogeneous. Morphologic subclassifications have been proposed with a presumptive relationship to immunologic phenotype. Six histologic types were studied, four of presumed follicular origin (large cleaved, large non-cleaved, mixed follicular center cell, and blastic) and two of presumed nonfollicular origin (pleomorphic pyroninophilic and pleomorphic convoluted). Two of these follicular subtypes were found to be associated with the frequent presence of B-cell markers; large non-cleaved, six of seven; and blastic, four of six. However, four of nine T-cell lymphomas were misclassified as lesions of follicular center cell type, indicating the difficulty of distinguishing some convoluted cells of T-cell lymphoma from irregularly cleaved cells of follicular lymphoma. Pleomorphic pyroninophilic or B-immunoblastic morphology was associated with B-cell markers in only two of six cases; two additional cases had T-cell markers, one had histocytic markers and in one case, no markers were demonstrable. Thus, this morphology may reflect a common pathway of transformed lymphoid cells. Some cases of T-cell origin could be recognized by the striking pleomorphic convoluted histology (3 of 5 cases) but morphologic overlap with pleomorphic B-cell tumors, particularly transformed nodular lymphomas, posed a problem. This histopathologic subclassification correctly predicted immunologic phenotype in only 61% of cases, suggesting that in diffuse non-Hodgkin's lymphomas, histologic appearance alone may not be a reliable indicator of immunologic surface markers. (Author abstract) (17 Refs)

18. A STUDY OF SURFACE MARKERS IN NON-HODGKIN'S LYMPHOMA OF THE HEAD AND NECK.

Yamanaka N
Dept. Otolaryngology, Sapporo Medical Coll., Sapporo, Japan
Jibi Inkoka; 53(11):1057-1068 1981

Cell surface markers of 14 cases of non-Hodgkin's lymphoma of the head and neck, especially of Waldeyer's ring origin, were studied with various surface markers, especially by using anti-human B lymphocyte serum (ABS) and anti-human T lymphocyte serum (ATS), which were rendered specific for human B lymphocytes and human peripheral T lymphocytes respectively. An immunofluorescent study with ABS and ATS enabled us to demonstrate the histologic localization of normal or neoplastic B and T cells in preserving the original structure of tumor tissues. The proportion of cell types in non-Hodgkin's lymphoma was B cell type 71% and T cell type 29%. The relationships among cell types, clinical characteristics, and histologic findings were also investigated. Patients with B-lymphoma showed good response to radiation and chemotherapy, and were associated with good prognosis. On the other hand, patients with T-lymphoma were associated with poor prognosis and three of four patients were died within 8 months after diagnosis. B-lymphomas of diffuse type were found to be morphologically heterologous, whereas the histology of T-lymphomas was relatively uniform, ie, in three of four cases tumor cells showed the highly pleomorphic features of nucleus. (Author abstract) (22 Refs) (In JPN)

19. A COMBINED MORPHOLOGIC AND IMMUNOLOGIC APPROACH TO THE DIAGNOSIS OF GASTROINTESTINAL LYMPHOMAS. I. MALIGNANT LYMPHOMA OF THE STOMACH (A CLINICOPATHOLOGIC STUDY OF 22 CASES).

Seo IS, Binkley WB, Warner TF, Warfel KA
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Cancer; 49(3):493-501 1982

Twenty-two cases of primary gastric non-Hodgkin's lymphoma, which occurred over a 20-yr period, were reviewed. Eighteen tumors were studied using an immunoperoxidase method, and the presence of intracytoplasmic monoclonal immunoglobulin (Ig) in 9 (50%) suggested a B-cell origin. Four tumors (22%) contained intracytoplasmic muramidase (lysozyme), suggesting a true histiocytic origin. Five tumors (28%) did not contain immunoglobulin or muramidase. The muramidase-positive 'true histiocytic lymphoma' could not be differentiated from histiocytic lymphoma of lymphocytic origin using light microscopic examination alone. The patients with B-cell lymphoma survived significantly longer than patients in the other two groups. The differentiation between true histiocytic lymphoma and other conditions is discussed. (Author abstract) (29 Refs)

20. ULTRASTRUCTURE OF ADULT T-CELL LEUKEMIA/LYMPHOMA.

Eimoto T, Mitsui T, Kikuchi M
Dept. Pathology, Fukuoka Univ. Sch. Medicine, Nanakuma 34, Nishi-ku, Fukuoka, 814-01, Japan
Virchows Arch [Cell Pathol]; 38(2):189-208 1981

Eighteen cases of adult T-cell leukemia/lymphoma (ATLL) in Japan were analyzed by electron microscopy and compared with 5 cases of B-lymphoma and well-established groups of T-lymphomas (4 cases of T-lymphoblastic lymphoma and 2 cases of Sezary syndrome). Five hundred cells in each case, categorized ultrastructurally as to the cellular size and nuclear shape, showed an essentially pleomorphic cellular distribution in ATLL in remarkable contrast with the monomorphism of B-'histiocytic', B-well-differentiated lymphocytic, and T-lymphoblastic lymphomas. Some B-lymphomas and Sezary syndrome also showed pleomorphism. Cases of ATLL were classified according to the predominant cells and degree of nuclear irregularity, which delineated a spectrum of node-based, peripheral T-cell neoplasms probably encompassing T-immunoblastic sarcoma, T-zone lymphoma, as well as multilobated T-cell lymphoma. The characteristic fine structure of ATLL, in comparison with that of B-lymphomas, included slight to marked nuclear irregularity with convoluted-shape predominance, a speckled chromatin pattern of the large cells, prominent lysosomes, and glycogen accumulation in addition to the difference in cellular distribution. Although T-lymphoblastic lymphoma and Sezary syndrome shared some of these features, the ultrastructural differentiation of ATLL from them seems to be possible. (Author abstract) (31 Refs)

21. CLONAL CHARACTERISTICS OF CUTANEOUS T CELL LYMPHOMAS: CYTOGENETIC EVIDENCE FROM BLOOD, LYMPH NODES, AND SKIN.

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J Invest Dermatol; 78(1):69-75 1982

Chromosome studies were done on mitogen-stimulated lymphocytes from one or more tissues (blood, lymph nodes, skin lesions) in 15 patients with mycosis fungoides or Sezary syndrome. A cytogenetically abnormal clone was found in 10 individuals, including 6 with data from several tissues. In four cases the same aberrant clone was identified in a skin lesion as well as in blood and/or lymph node. the abnormal chromosome patterns ranged from hypodiploid to hypertetraploid, and there was no evidence of unrelated karyotypically-altered lines at different sites. A 6q- chromosome, previously reported in acute lymphocytic leukemia, was found in two patients. The results support the concept that cutaneous T cell lymphomas (CTCL) are clonal disorders, presumably unifocal in origin, with the skin lesions populated by cells from the same neoplastic clone that involves lymph nodes and blood. (Author abstract) (17 Refs)

MALIGNANT LYMPHOMA: CLINICAL IMMUNOLOGY AND IMMUNOTHERAPY

22. IMMUNOLOGICAL SUBSETS IN HUMAN B-CELL LYMPHOMAS.

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Scand J Immunol; 14(5):481-492 1981

Fifty human B-cell lymphomas have been studied with regard to surface markers (surface immunoglobulins (sIg) and complement receptors (CR)), capping of sIg, and relative amounts of sIg by single-cell flow cytometry. The results show that these lymphomas can be subdivided into distinct immunological subsets. Whereas one histological subgroup (lymphocytic) consisted of only one immunological subtype, others were heterogeneous with regard to immunological subtypes. This was most striking in nodular lymphomas of germinal center cell origin (centroblastic/centrocytic). Our studies provide further evidence for the existence of a large number of subsets in the B-cell compartment of the immune system. sIgD was only found in association with sIgM. The relative amounts of sIgD varied, especially in nodular lymphomas. A discrepancy between capping of sIgM and sIgD was also found in some lymphomas belonging to this group. These findings together with other observations suggest that sIgD plays a role in B-cell maturation and differentiation events taking place in germinal centers and becomes lost during this process. A close association was found between the presence of CR and capping of sIgM but not capping of sIgD or sIgG. Nodular lymphomas expressing sIgG only, lacked CR. These findings suggest that CR may become lost during maturation and differentiation processes also taking place in germinal centers. Lymphoplasmacytoid lymphomas, which show morphological evidence of differentiation towards plasma cells, could be subdivided into three immunological subsets, indicating that plasma cell maturation may take place from different subsets of B cells. (Author abstract) (39 Refs)

23. IMMUNO-HISTOLOGICAL ANALYSIS OF BONE MARROW INVOLVEMENT IN LYMPHOPROLIFERATIVE DISORDERS.

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Br J Haematol; 50(1):95-100 1982

Cryostat sections from bone marrow biopsies submerged in gum-sucrose solution and snap-frozen can be stained with various antisera to detect both the membrane and cytoplasmic antigens on normal and malignant populations in their tissue environments. This technique seems to be the method of choice to analyze the degree of BM involvement in cases of non-Hodgkin's lymphoma where conventional histology provides equivocal results. The uniform expression of only one type of light chain in B lymphoma and the analysis of the T cell infiltrate in T-CLL using monoclonal antibodies is demonstrated. (Author abstract) (9 Refs)

24. BLOOD LYMPHOCYTE SUBPOPULATIONS IN MYCOSIS FUNGOIDES AND THEIR FUNCTIONS IN VITRO.

Gu SQ, Petrini B, Von Stedingk LV, Thyresson N, Wasserman J

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Acta Derm Venereol (Stockh); 61(6):487-490 1981

T-lymphocyte subpopulations, PWM stimulated in vitro Ig production by mononuclear cells, and spontaneous cell-mediated cytotoxicity (SCMC) were determined in patients with Mycosis fungoides (MF) as well as in sex- and age-matched normal controls. We were able to confirm our earlier findings of a significantly higher frequency of T-lymphocytes with Fc-receptors for IgG (Tg cells) and a proportion of T lymphocytes with Fe receptors for IgM (Tm cells) not significantly differing from normal controls. As defined by monoclonal antibodies, the proportion of T-helper cells (Leu3A) was significantly lower, whereas the T-suppressor cells (Leu2A) were in the range of normal controls. The PWM stimulated and spontaneous Ig synthesis in vitro was lower in MF patients whereas there was no difference in the SCMC activity, in comparison with normal controls. The lower frequency of T-helper cells in the peripheral blood may be explained by their migration to the skin. (Author abstract) (14 Refs)

MALIGNANT LYMPHOMA: CHEMOTHERAPY

25. PHASE II STUDY OF A HIGH-DOSE REGIMEN OF CYCLOPHOSPHAMIDE AND PREDNISOLONE IN ADVANCED NON-HODGKIN'S LYMPHOMA OF FAVORABLE HISTOLOGIC TYPE.

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Cancer Treat Rep; 66(2):377-380 1982

Fifty-seven courses of cyclophosphamide (2.5-5.0 g/m(2)) and prednisolone (1.0 g /m2 x 5) were given to 22 patients with advanced stage IV non-Hodgkin's lymphoma of favorable histology. Six patients (27%) had a complete response (CR) (median duration, 10.1 months), and six (27%) had a partial response (median duration, 3.0 months). All patients in whom CR was achieved had a previous disease pattern of remission and relapse, and no patient refractory to previous therapy had a CR. This association of CR to disease pattern was statistically significant (P less than 0.0001). There was no difference in the survival of complete and partial responders. There was a trend to a higher response rate and statistically significant survival advantage (P less than 0.05) for patients with the nodular histologic types. The transient nature of response and the toxicity of the regimen, with four therapy-related deaths, render it unsuitable as routine therapy. (Author abstract) (7 Refs)

26. THERAPEUTIC RESULTS IN CHILDREN WITH NON-HODGKIN'S LYMPHOMA TREATED ACCORDING TO THE STANDARD PROTOCOL (LSA2L2).

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Pediatr Pol; 56(9):1071-1077 1981

The results of chemotherapy of 16 children (12 boys and 4 girls, 1-14 yr old) with non-Hodgkin's lymphoma (NHL) are reported. Lymphoblastic B-cell lymphoma was diagnosed in four patients, lymphoblastic T-cell lymphoma in two, immunoblastic lymphoma in three, convoluted lymphoblastic lymphoma in one, Burkitt's lymphoma in three, malignant histiocytosis in one, type U NHL in one and other NHL in one. Two patients were in Stage I, two in Stage II, four in Stage III and four in Stage IV. Remission induction therapy consisted of cyclophosphamide (CP: 1,200 mg/square m (m2), day 1), prednisone (PR: 60 mg/m2, days 3-31), vincristine (VCR: 1.5-2.0 mg/m2, days 3, 10, 17 and 24), methotrexate (MTX: 6.25 mg/m2 intrathecally, days 5, 27 and 30), and rubidomycin (RBC: 60 mg/m2, days 12 and 13). Consolidation therapy, started 3-5 days after remission induction therapy, consisted of cytosine arabinoside (ara-C: 150 mg/m2 iv on 5 consecutive days of the wk for 4 wk), 6-thioguanine (6-TG: 75 mg/m2 po according to same schedule as ara-C), L-asparaginase (60,000 U/m2 iv), and lomustine (60 mg/m2 iv). Maintenance therapy consisted of 6-TG, CP, RBC, MTX, VCR and ara-C. The patients were followed up for 1-40 mo. The fate of one patient is unknown. Seven children died within 1-10 mo (av 4.5 mo): the cause of death was dissemination of the malignant process in four cases, associated complications in three. The other eight patients have been alive for 1-40 mo (av 13.5 mo). Six of these eight patients are in continuing remission, one is alive with recurrence, and another is under remission induction therapy. The most severe side-effects included bone marrow depression with pronounced leukopenia and granulocytopenia. The findings indicate that the LSA2L2 protocol used is very aggressive but prolongs survival. (13 Refs) (In POL)

MALIGNANT LYMPHOMA: RADIOTHERAPY

27. THYROID FUNCTION AFTER MANTLE FIELD RADIATION THERAPY.

Dahnert W, Kutzner J, Grimm W

Universitatsklinik Mainz, Langenbeckstr. 1, D-6500 Mainz, W. Germany

Strahlentherapie; 157(8):499-507 1981

Forty eight patients with malignant lymphoma received a 60Co-radiation of 30 to 50 Gy using the mantle field technique. Thyroid function tests were performed 34 to 92 mo after radiation therapy. One patient developed myxedema, 10 (20.8%) had subclinical hypothyroidism and 6 (12.5%) latent hypothyroidism. The incidence of hypothyroidism after treatment of malignant lymphomas is summarized in a review of the literature. Discrepancies on the incidence of hypothyroidism were found, and their possible cause is discussed. Periodic examinations of all patients with thyroid radiation exposure are recommended. The examination can be limited to measurement of TSH concentration and palpation of the thyroid for nodules. (Author abstract) (38 Refs) (In GER)

28. MALIGNANT LYMPHOMA WITH PRIMARY INVOLVEMENT OF WALDEYER'S RING.

Tang W, Yu L, Zhang Y

Cancer Hosp., Shanghai First Medical Coll., Shanghai, People's Republic of China

Zhonghua Zhongliu Zazhi; 3(2):113-116 1981

Radiotherapy and clinicopathological findings are described for 145 cases (95 males, 50 females; 3-79 yr old) of primary malignant lymphoma involving the Waldeyer's ring. There were 85 cases of reticulum cell sarcoma, 56 cases of lymphosarcoma, 1 case of Hodgkin's disease and 3 unclassified. Major primary organ sites were the tonsils (107 cases) and the nasopharynx (33 cases). X-ray irradiation or Co-60 teletherapy, with a total tumor dose 4,000-6,000 rad wsa given as a treatment. After treatment, 48% of patients survived over 5 yr and 46% over 10 yr. Tumor recurrence rate within the irradiated region was only 2% (3/145). However, incidences of metastasis and recurrence outside the irradiated region were high. The most common metastatic sites were the abdominal, inguinal and cervical lymph nodes, with abdominal metastatic rate reaching 15% in this series, or 38% among metastatic cases. Visceral metastasis involved mainly the liver and stomach. Tumor staging and its relation to radiotherapy are discussed. (7 Refs) (In CHI)

29. THE IMPORTANCE OF AN OVERALL RADIOTHERAPY FOR THE PROGNOSIS OF THE CENTROBLASTIC-CENTROCYTIC LYMPHOMA AND THE BRILL-SYMMERS DISEASE, RESPECTIVELY. RESULTS REACHED AT FREIBURG FROM 1965 TO 1979.

Slanina J, Wannenmacher M, Widmaier S

Abteilung Strahlentherapie, Universitatsklinik Frieburg, Hugstetterstr. 55, D-7800 Freiburg, W. Germany

Strahlentherapie; 157(8):516-523 1981

Thirty-nine patients suffering from the Brill-Symmers disease or a centroblastic-centrocytic lymphoma who had been treated between 1965 and 1979 at the Radiotherapy Department of Freiburg i Br were analyzed retrospectively with regard to therapeutic results and prognostic factors. In 90% of the Stages I to III (30 patients), a total remission was reached by primary radiotherapy. In eight of these patients (27%), a recurrence appeared after 7 to 53 mo following the beginning of the treatment; in fact, they were observed only in lymph node regions which had not been irradiated before (neither for therapeutic reasons nor as an adjuvant measure). A dose of 25 Gy was found to be sufficient to destroy the focus. The 5-yr survival rate of the whole group of patients (Stages I to IV) was 52%, the survival rate without recurrences was 42%. A comparison of the loco-regionally delimited Stages I to III showed that the best therapeutic results were reached in patients with supra- and infradiaphragmatic manifestations of Stage III. These patients had received the most integral systemic irradiation. With respect to these results as well as to the recurrences observed only in non-irradiated lymph node regions, we concluded that primary radiotherapy of the first stages should - beyond the principles of the extended field method binding hitherto - comprise the total lymphatic system in the form of TLI (total lymphatic irradiation). (Author abstract) (21 Refs) (In GER)

MALIGNANT LYMPHOMA: MULTIMODAL THERAPY

30. CENTRAL NERVOUS SYSTEM INVOLVEMENT IN NON-HODGKIN'S LYMPHOMA: AN ANALYSIS OF 105 CASES.

Mackintosh FR, Colby TV, Podolsky WJ, Burke JS, Hoppe RT, Rosenfelt FP, Rosenberg SA, Kaplan HS

(c/o Rosenberg) Div. Oncology, Stanford Univ. Medical Center, Room S025, Stanford, CA, 94305

Cancer; 49(3):586-595 1982

Records of 105 patients with central nervous system (CNS) lymphoma were analyzed in order to better define the incidence, setting, and management of CNS lymphoma and the role for CNS prophylaxis. Survival was best for patients under 30 years of age treated with whole-brain irradiation and intrathecal (IT) chemotherapy whose CNS involvement was an isolated event (median survival time, 1.8 years). Survival was worst for patients over 30 years of age whose CNS invasion occurred at a time of progressive systemic lymphoma (median time 10 weeks if treated with whole-brain irradiation with or without IT chemotherapy). The risk of CNS invasion was greatest for those with lymphoblastic lymphoma. Among patients with Stage IIE, III, or IV histiocytic lymphoma, the risk of CNS involvement was greatest for those with progressive or relapsing disease or involvement of the testes, peripheral blood, or epidural space of the spinal cord. (Author abstract) (38 Refs)

31. CNS INVOLVEMENT IN NON-HODGKIN'S LYMPHOMAS. CLINICAL ASPECTS AND THERAPY.

Hennemann HH, Ranft K, Weiss A, Mantel W, Lengfelder E

III. Medizinische Klinik, Klinikum Mannheim der Universitat Heidelberg, Wiesbadener Str. 7-11, D-6800 Mannheim 31, W. Germany

MMW; 123(51/52):1975-1977 1981

Incidence, manifestations, and treatment of central nervous system (CNS) involvement associated with the occurrence of non-Hodgkins lymphoma (NHL) were investigated in 58 patients with NHL (excluding chronic lymphatic leukemia). CNS involvement was detected in three patients (2 women and 1 man, 57-65 yr old) with NHL of low malignancy and in three patients (2 men and 1 woman, 15-72 yr old) with NHL of high malignancy. The manifestations of the CNS involvement included meningitis, cranial nerve involvement, intracerebral or intracerebellar foci, or a combination of these symptoms. The interval between treatment of the NHL and occurrence of the CNS symptoms ranged from 5 wk to 4 yr; shorter intervals were found for patients with highly malignant NHL. The CNS involvement was treated through intrathecal administration of methotrexate (MTX) in 4/6 patients and by MTX plus cranial irradiation in 1/6 patients; four of these five patients had favorable responses to treatment. The CNS involvement of the remaining 1/6 patients was treated by symptomatic therapy. Two patients (including the one who received symptomatic treatment) were alive at the time of this report. One patient committed suicide 6 yr after her initial treatment. The survival times of the remaining three patients were 10.5, 16, and 23 mo; two of these patients had highly malignant NHL. Preventive treatment (irradiation and intrathecal MTX) is recommended for all patients with lymphoblastic lymphoma and all patients with highly malignant NHL in Stage IV B. (9 Refs) (In GER)

32. MANAGEMENT OF PRIMARY GASTRIC LYMPHOMA.

Shiu MH, Karas M, Nisce L, Lee BJ, Filippa DA, Lieberman PH

Dept. Surgery, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021

Ann Surg; 195(2):196-202 1982

A retrospective study of 51 patients treated for primary gastric lymphoma was made to evaluate the influence of clinicopathologic features and the method of treatment on survival. The lymphocytic type of tumor showed a higher survival rate than the histiocytic type. Tumors that involved only the gastric wall resulted in a 5-yr survival rate of 62%, as compared with 50% for tumors that involved also the adjacent gastric lymph nodes, and 25% for those involving the distant gastric lymph nodes. Treatment by subtotal, total, or extended forms of gastric resection without postoperative radiation gave a 5-yr survival rate of 33%. Resection followed by radiation yielded a higher survival rate of 67%. The best results were obtained in 13 patients who received higher doses of radiation: 11 (85%) survived 5 or more yr. One-third of the patients developed manifestations of systemic malignant lymphoma after curative therapy. These observations suggest a planned multimodal therapeutic program for this disease. (Author abstract) (22 Refs)

33. HISTOPATHOLOGIC SUBCLASSIFICATION OF DIFFUSE HISTIOCYTIC LYMPHOMA AND RESPONSE TO THERAPY.

Stryker JA, Abt AB, Eyster ME, Lowman JG

Div. Radiation Oncology, M.S. Hershey Medical Center, Pennsylvania State Univ., Hershey, PA, 17033

Radiology; 142(2):501-506 1982

In 55 patients with diffuse histiocytic lymphoma (Stages I-IV), the disease was subclassified as large cleaved-cell (17 patients), large noncleaved-cell (12 patients), mixed follicular-center cell (14 patients), blastic (6 patients), and pleomorphic pyroninophilic (6 patients). Two-year survival rates for these subclasses were 47%, 42%, 64%, 17%, and 33%, respectively, suggesting that histopathologic subclass is an important prognostic factor in diffuse histiocytic lymphoma. The mean tumor dose that produced local control in 22 patients who were treated with radiation therapy alone was 4,834 rad (48.34 Gy), whereas the mean tumor dose for local control when chemotherapy was used in combination with radiation therapy (16 patients) was 3,679 rad (36.79 Gy). This suggests that when chemotherapy is used with radiation therapy, a lower tumor dose will be sufficient to achieve local control than when radiation therapy is used alone. In addition, 43% of the patients who presented with an intra-abdominal primary lymphoma experienced local failure following treatment. It is recommended that patients who present with an abdominal primary tumor be treated aggressively with combined modality therapy whenever feasible. (Author abstract) (18 Refs)

MALIGNANT LYMPHOMA: CASE REPORTS

34. CHEMOTHERAPY FOR LYMPHOMA IN A PATIENT WITH COMMON VARIABLE IMMUNODEFICIENCY: CASE REPORT, LITERATURE REVIEW, AND RECOMMENDATIONS FOR CHEMOTHERAPY IN IMMUNODEFICIENT PATIENTS.

Gelmann E, Anderson T, Jaffe E, Broder S
Medical Branch, NCI, NIH, Building 10, Bethesda, MD, 20205
Arch Intern Med; 142(1):90-92 1982

A man with long-standing common variable hypogammaglobulinemia was treated with chemotherapy and local radiation for diffuse mixed lymphoma. He continues in complete remission 42 months after the completion of therapy. Vigorous therapy for lymphoma can be used in the face of preexistent immunodeficiency. Complete staging and appropriate combination chemotherapy or radiation therapy should be carried out for lymphomas that occur in certain immunodeficient patients. (Author abstract) (15 Refs)

35. CONCENTRATIONS OF FREE AMINO ACIDS AND OTHER BLOOD COMPONENTS IN A LYMPHOMA PATIENT DURING INTENSIVE HEMODIALYSIS.

Riley V
Pacific Northwest Res. Foundation, Seattle, WA
Nutr Cancer; 2(3):165-180 1981

A method was examined whereby L-asparagine can be physically removed from patient's circulating blood by hemodialysis. The study was performed on a 58-yr-old white male with lymphoblastic lymphosarcoma. L-asparaginase was used as a therapeutic enzyme to selectively destroy asparagine-dependent cancer cells. Approx 1200 mg, the equivalent of the patient's total amino acid pool, was removed every 100 minutes while the patient was on the artificial kidney. The dialyzer was not capable to completely overcome the endogenous amino acid influx of the patient. The combined data indicate that hemodialysis is theoretically capable of removing specific amino acids to a therapeutic level, but that the clearance efficiency of the artificial kidney must be significantly increased or the endogenous amino acid influx must be effectively blocked before hemodialysis can be successfully applied to cancer patients. The malignant lymphocyte population was strikingly increased during dialysis but returned to the original levels when dialysis was temporarily discontinued. The presence of a nonprotein inhibiting factor capable of suppressing an increase in the peripheral malignant lymphocyte population could be an explanation. The behavior of the factor during dialysis indicated that the mol wt was relatively low, possibly less than 500. (26 Refs)

36. IMMUNOBLASTIC LYMPHOMA OF SMALL INTESTINE COMPLICATING LATE-ONSET IMMUNODEFICIENCY.

Gonzalez-Vitale JC, Gomez LG, Goldblum RM, Goldman AS, Patterson M
Dept. Pathology, Union Hosp., Elkton, MD, 21921
Cancer; 49(3):445-449 1982

A malignant lymphoma of the small bowel developed in a 75-year-old woman who had severe late-onset hypogammaglobulinemia with intestinal malabsorption and nodular lymphoid hyperplasia. The tumor arose in the midst of the abnormal lymphoid follicles and appeared to be of B-immunoblastic type. Immunoperoxidase staining, however, failed to reveal immunoglobulins in the tumor cells. In vitro immunologic studies showed that immunoglobulin production by the patient's peripheral lymphocytes had decreased and that this decrease was mediated by hydrocortisone-sensitive suppressor cells. These findings suggest that nodular lymphoid hyperplasia of the intestine in the context of severe immunodeficiency is a premalignant condition. (Author abstract) (18 Refs)

MALIGNANT LYMPHOMA: SELECTED REPORTS ON ETIOLOGY AND EPIDEMIOLOGY

37. LYMPHOMAS AND LEUKEMIAS IN THE RELATIVES OF PATIENTS WITH MYCOSIS FUNGOIDES.

Greene MH, Pinto HA, Kant JA, Siler K, Vonderheid EC, Lamberg SI, Dalager NA

Environmental Epidemiology Branch, NCI, Landow C3-07, Bethesda, MD, 20205

Cancer; 49(4):737-741 1982

Of 526 consecutive patients with cutaneous T-cell lymphomas, 21 had first-degree relatives with lymphoproliferative or hematopoietic malignancies. Twenty-nine such tumors occurred in the 21 kindreds. Hodgkin's disease accounted for one-third of this total, with various leukemias (11 cases), non-Hodgkin's lymphoma (5 cases), and multiple myeloma (3 cases) comprising the remainder. These data suggest that genetically-determined immunoregulatory abnormalities may represent a shared pathway of oncogenesis in diverse lymphoproliferative and hematopoietic malignancies. (Author abstract) (25 Refs)

38. TRANSFORMATION OF PARAPSORIASIS INTO MYCOSIS FUNGOIDES.

Kalamkarian AA, Sych LI, Orazymbetova ZhA

Dept. Dermatology, Central Dermatological-Venereological Inst., Moscow, USSR

Vestn Dermatol Venerol; (11):8-13 1981

Clinical and morphological manifestations of parapsoriasis (PP) are reviewed with special emphasis on PP transformation into mycosis fungoides (MF). Characteristic features of PP transformation include enlargement of lesions, increase of the degree of infiltration in the foci, changes of the color of the foci, development of itching, and enlargement of the peripheral lymph nodes. Early stages of MF were characterized by the increase of DNA and RNA content and by high activity of lactate dehydrogenase, glucose-6-phosphate dehydrogenase, succinate dehydrogenase, and malate dehydrogenase. In contrast with MF, PP was characterized by a relatively low metabolic activity. (30 Refs) (In RUS)

MALIGNANT LYMPHOMA: SELECTED PRE-CLINICAL STUDIES

39. LYMPHOCYTE DIFFERENTIATION AND MALIGNANT LYMPHOMA.

Kikuchi K, Ishii Y, Koshiba H
Dept. Pathology, Sapporo Medical Coll., Sapporo, Japan
Nippon Ketsueki Gakkai Zasshi; 44(7):1384-1394 1981

Diagnostic and immunopathologic application of xenoantisera against human normal and neoplastic T and B cells, immunochemical characterization of lymphocyte surface antigens, establishment of B cell hybridomas secreting monoclonal antibodies to lymphocyte differentiation antigens, and analogy of mouse to human lymphocyte differentiation antigens and their distribution in normal and neoplastic immune systems are discussed. Lymphocyte differentiation and malignant lymphomas were studied using 50 hematopoietic cell lines. Cell lines were used to determined to what kind of differentiation stage the antigen belonged, the differentiation stages having been defined with xenoantisera or monoclonal antibodies. Stages of lymphocyte ontogeny were determined with the use of lymphocyte markers, differentiation antigens defined by monoclonal antibodies and conventional antisera. Results showed that lymphoid malignancies reflect the same degree of heterogeneities in maturation as seen in normal lymphocyte differentiation, and each of them can belong to a specified compartment. Relationship among possible compartments of T and B cell differentiation, leukemia-lymphomas and cell surface markers is presented. Malignant lymphomas and leukemias are easily diagnosed and classified according to their cell surface phenotype, and may be considered as clonal expansions of the specific normal anatomic and functional components of the immune system under 'frozen' differentiation. Surface phenotypes might reflect the clinical and pathologic expressions in patients with malignant lymphomas and leukemias with these phenotypes. (15 Refs)

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HODGKIN'S DISEASE: DIAGNOSIS AND STAGING

1. A COMPARISON OF COMPUTED TOMOGRAPHY AND LAPAROTOMY IN STAGING LYMPHOMAS.

Blackledge G
Cancer Res. Campaign, Dept. Medical Oncology, Manchester Univ., Wilmslow Road, Manchester M20 9BX, England
Nouv Rev Fr Hematol; 23(1):9-12 1981

The role of computed tomography (CT) in staging lymphoma was compared with laparotomy in 105 cases of Hodgkin's disease and 30 non-Hodgkin's lymphomas. CT and laparotomy agreed in 26/30 (87%) of the patients with non-Hodgkin's lymphomas. CT detected unsuspected disease in the retrocrural area in nine patients and failed to detect diffuse lymphomatous infiltration of the liver in four cases found at laparotomy. CT detected splenic abnormalities in 5/6 cases, but all were enlarged. Mesenteric node enlargement was seen in eight cases with CT, while only three cases were seen at laparotomy. Laparotomy revealed evidence of Hodgkin's disease in 42/105 cases; CT did not detect disease in 31 of these cases. In 2 of 11 cases in which CT and laparotomy agreed, CT detected additional disease in the left para-aortic region. Abnormal spleens were detected in only 6/365 cases by CT. Laparotomy did not confirm seven cases with abdominal disease. CT did not detect 18 involved lymph nodes found at laparotomy. CT predicted liver involvement in 5/11 positive cases; three false-positive results were found. Thus, laparotomy is superior in staging Hodgkin's disease and is the definitive investigation for abdominal lymphoma. CT cannot detect involved spleens unless they are enlarged, also cannot detect normal-sized involved nodes in the upper abdomen, and is inaccurate in predicting liver involvement. (9 Refs)

2. PROGNOSTIC VALUE OF SERUM LACTIC DEHYDROGENASE LEVEL IN HODGKIN'S DISEASE.

Schilling RF, McKnight B, Crowley JJ
Dept. Medicine, Univ. Wisconsin-Madison, 600 Highland Ave., Madison, WI, 53792
J Lab Clin Med; 99(3):382-387 1982

The serum LDH level determined at time of diagnosis provides important prognostic information about patients with Hodgkin's disease. The median survival of patients with a normal value was 129 months, whereas those with elevated values had a median survival of only 39 months. The prognostic power of LDH persisted after adjustment of age, symptom class, stage, or histology. When the Cox proportional hazards regression method was used to simultaneously adjust for age, histology, symptom class, and stage, elevated enzyme levels still were correlated with short survival. (Author abstract) (15 Refs)

3. MORPHOMETRICAL ANALYSIS OF T- AND B-CELL COMPARTMENTS OF SPLEENS IN HODGKIN'S DISEASE.

Timens W, Koudstaal J, Poppema S
(c/o Poppema) Dept. Pathology, Univ. Groningen, Oostersingel 63, NL-9713 EZ Groningen, The Netherlands
Virchows Arch [Cell Pathol]; 38(3):291-296 1982

One possible explanation for the defective cellular immunity in Hodgkin's disease is an abnormal distribution of T lymphocytes. To study this possibility a morphometric analysis of T- and B-areas in non involved and involved spleens of patients with Hodgkin's disease was undertaken. We found tha t in involved spleens a significant reduction of the T dependent area could be demonstrated. We concluded that this reduction is caused by an abnormal distribution of T lymphocytes in the spleen and may partly explain the defects in cellular immunity. In addition, the absence of overlap between the T/B area ratios of involved and non-involved spleens suggests, that a prediction on involvement of spleen can be made by morphometrical analysis of a small, random taken non-involved area. (Author abstract) (13 Refs)

HODGKIN'S DISEASE: CLINICAL IMMUNOLOGY AND IMMUNOTHERAPY

4. IN SITU IMMUNOLOGIC CHARACTERIZATION OF CELLULAR CONSTITUENTS IN LYMPH NODES AND SPLEENS INVOLVED BY HODGKIN'S DISEASE.

Poppema S, Bhan AK, Reinherz EL, Posner MR, Schlossman SF
(c/o Bhan) Dept. Pathology, Massachusetts General Hosp., Boston, MA, 02114
Blood; 59(2):226-232 1982

The cellular constituents in lymph nodes and spleens of patients with Hodgkin's disease were studied with a series of monoclonal antibodies directed against human thymocyte, peripheral T-cell, and Ia antigens. Utilizing both an immunoperoxidase technique on frozen tissue sections and indirect immunofluorescence on cell suspensions, we found that a majority of lymphocytes were T cells, since they stained with anti-T1 and anti-T3 antibodies, which react with all peripheral T cells. In addition, most of these cells were reactive with anti-T4 antibody, which defines the helper/inducer T-cell population, whereas only a minority of cells stained with anti-T5 and anti-T8 antibodies, which are reactive with suppressor/cytotoxic T cells. Moreover, a large proportion of T cells expressed T10 antigen, which is found on activated T cells. A minority of the T cells also expressed Ia antigen(s), again suggesting that some of the T cells are activated. In contrast, the Reed-Sternberg cells did not react with any of these anti-T-cell antibodies or with anti-IgM antiserum, but displayed strong membrane and cytoplasmic staining with anti-Ia antibody. Taken together, these findings suggest that Reed-Sternberg cells are not of T-cell lineage but may be derived from antigen-presenting reticulum cells in the thymus-dependent areas of lymphoid tissues; these cells are normally associated with T4 cells. (Author abstract) (40 Refs)

5. POLYMORPHONUCLEAR FUNCTIONS IN HODGKIN'S DISEASE PATIENTS AT DIAGNOSIS, IN REMISSION, AND IN RELAPSE.

Corberand J, Benchekroun S, Nguyen F, Laharrague P, Pris J
Laboratoire Central d'Hematologie CHU Rangueil, 31054 Toulouse Cedex, France
Cancer Res; 42(4):1595-1599 1982

Five tests investigating different aspects of the nonspecific defense mechanisms including capillary tube random migration, particle ingestion activity, quantitative and histochemical nitroblue tetrazolium dye reduction by polymorphonuclear neutrophils, and serum lysozyme concentrations we re performed in 46 patients with Hodgkin's disease. The anomalies observed in the active stage of the disease consisted of a decreased random migration, a higher level of serum lysozyme, and an increased nitroblue tetrazolium reduction by resting phagocytes associated with a decrease in nitroblue tetrazolium reduction by stimulated phagocytes. The particle ingestion activity was normal. The serum lysozyme assay was the only test observed to normalize in the group of patients in remission. Its determination, therefore, offers an additional means of evaluating disease activity. (Author abstract) (45 Refs)

6. NEUTROPHIL FUNCTION DURING CHEMOTHERAPY FOR HODGKIN'S DISEASE.

Gandossini M, Souhami RL, Babbage J, Addison IE, Johnson AL, Berenbaum MC
(c/o Souhami) ICRF Human Tumor Immunology Group, Univ. Coll. Hosp., London WC1E 6JJ, England
Br J Cancer; 44(6):863-871 1981

Simultaneous measurement of neutrophil migration, phagocytic activity, candidacidal and bactericidal activity were made during quadruple chemotherapy of advanced Hodgkin's disease (HD). Measurements were also made in normal individuals, hospital patients not on chemotherapy, untreated patients with advanced HD and patients off chemotherapy for over a year. Neutrophil migratory activity was usually normal in untreated HD patients and those on chemotherapy, but greater than 20% of all tests showed depressed values, some of which were corrected by plasma. Similar results were found with neutrophil phagocytosis. Abnormalities in these functions were found in both early and late cycles, but there was a tendency for migration to deteriorate during later chemotherapy cycles. Neutrophil candidacidal and bactericidal activity were frequently depressed in patients on treatment and there was deterioration in candidacidal activity during the chemotherapy cycle. These abnormalities of killing activity were frequently corrected in control plasma. Neutrophil function is normal in most patients with advanced HD and in patients in remission. In a minority of patients on treatment there are maked functional defects, especially in killing activity. These defects are partly cell-associated and partly plasma-related. Susceptibility to infection during chemotherapy of HD may be partly due to defective neutrophil function. (Author abstract) (14 Refs)

7. IMPAIRED AUTOLOGOUS MIXED LYMPHOCYTE REACTIVITY IN HODGKIN'S DISEASE.

Begemann M, Claas G, Falke H
Med. Univ.-Klinik, Emil-Mannkopff-Str. 1, D-3550 Marburg, W. Germany
Klin Wochenschr; 60(1):19-26 1982

In patients with Hodgkin's disease, the impaired immune reactivity, especially of the thymus dependent system, is well established. The decreased immune response of the lymphocytes from the peripheral blood contrasts to an increased lymphocytopoiesis in the lymphatic organs with a hyper plasia of these tissues. We studied the reactivity of peripheral T lymphocytes from 20 patients with Hodgkin's disease and 26 healthy control persons against autologous and allogeneic non T cells respectively in the mixed lymphocyte culture (MLC). Our experiments show an extremely depressed autologous mixed lymphocyte reactivity (MLR) of T lymphocytes from patients with Hodgkin's disease compared to those from normal donors. In the allogeneic MLC, the proliferation of the patients' T cells was stronger than in the autologous MLC, but significantly lower than the proliferation of normal T lymphocytes when stimulated by normal non T cells. Patients' non T cells stimulated T lymphocytes from healthy donors as well as non T lymphocytes from normals did. Finally, the autologous MLR of normal lymphocytes was significantly suppressed by 18 of 23 sera from Hodgkin's patients when these sera were substituted for normal AB serum in the cultures. These results demonstrate an impaired function of T lymphocytes from patients with Hodgkin's disease in the autologous MLC and the presence of one or more factors in their serum which inhibit the proliferation of normal lymphocytes in the autologous MLC. The role of suppressor cells and their factors will be discussed. (Author abstract) (65 Refs)

HODGKIN'S DISEASE: CHEMOTHERAPY

8. LONG-TERM FOLLOW-UP OF TWO CHEMOTHERAPY PROTOCOLS IN HODGKIN'S DISEASE.

Pavlovsky S, Morgenfeld M, Somoza N, Magnasco J, Sackmann Muriel F, Cavagnaro F, Suarez A, Barros CA, Saslavsky J, Garay G, Palau M, Besuschio SC
Instituto de Investigaciones Hematologicas, Buenos Aires, Argentina
Medicina (B Aires); 41(Suppl):15-21 1981

Results of long-term follow-up of 303 patients with previously untreated Hodgkin's disease are presented; 160 of the patients received CVPP [cyclophosphamide (CY), vinblastine (VBL), procarbazine (PC), and prednisone (PRN)] and 143 received CVPP plus lomustine (CCVPP). Each cycle of therapy lasted 2 wk, followed by 2 wk rest, and was repeated six times during the induction phase, then given every 2 mo for the rest of the first yr, every 4 mo during th second yr, and every 6 mo during the third yr as maintainance. Patients with Stage I and Stage II disease received radiotherapy (4,000 rad) before starting polychemotherapy. Complete remission (RE) was obtained in 125/160 patients receiving CVPP and in 117/143 patients receiving CCVPP. Partial RE occurred in 19 and 14 patients, no RE in 4 and 3, and death within 6 mo in 12 and 9, respectively. Of the patients without symptoms in Stage I and Stage II (47), 87% achieved complete RE, lasting greater than 72 mo in 73%. Survival after 72 mo was 74% in patients achieving complete RE, 16% in those with partial RE, and only 5% in those without RE. CCVPP therapy was more effective than CVPP therapy, but the difference was not significant. (14 Refs)

HODGKIN'S DISEASE: CASE REPORTS

9. AUTOIMMUNE NEUTROPENIA IN HODGKIN'S DISEASE.

Hunter JD, Logue GL, Joyner JT
(c/o Logue) Section Hematology-Medical Oncology, Veterans Admin. Medical Center, Durham, NC, 27705
Arch Intern Med; 142(2):386-388 1982

A patient was profoundly neutropenic at the time of diagnosis of stage IIIB Hodgkin's disease. The neutropenia was not due to infection or bone marrow involvement by tumor. It did not respond to discontinuation of medication or to splenectomy, done for pathologic staging of Hodgkin's disease. The patient's serum contained abnormally increased granulocyte-binding antibody, which reacted with his own cells. The neutropenia resolved with high-dose prednisone therapy, and has not recurred after chemotherapy. Thus, immune neutropenia-as well as autoimmune hemolytic anemia and immune thrombocytopenic purpura-can be associated with Hodgkin's disease. Recognition and treatment of such immune processes assume major importance in planning cytotoxic therapy for the underlying malignancy. (Author abstract) (15 Refs)

HODGKIN'S DISEASE: SELECTED REPORTS ON ETIOLOGY AND EPIDEMIOLOGY

10. EPIDEMIOLOGICAL RISK FACTOR IN HODGKIN'S DISEASE.

Szelc S, Czech J, Kolosza Z

Oddzial 'A' Kliniki Radioterapii i Pracowni Epidemiologii Nowotworow, Oddzial Instytutu Onkologii, ul. Wybrzeze Armii Czerwonej 15, 44-100 Gliwice, Poland

Nowotwory; 31(2):169-174 1981

The possible risk factors of Hodgkin's disease (HD) were studied in 112 patients (53 men and 59 women) with HD and 101 control patients (48 men and 53 women) with solid tumors of various organs. The percentage of patients with HD from rural areas was 36.6%, that of the controls 21.8%, which may suggest that rural environment may play a role in the development of HD. No significant differences were found between the patients with HD and the controls in educational level and socioeconomic conditions. Considering the patients and controls who had been gainfully employed, 19.1% of the patients with HD and 21.8% of the control had been exposed to crude oil and mineral oils, 9.6% and 3.4%, respectively, to tar, asphalt and soot, and 6.4% and 4.6% to sawdust. No significant differences were found between the two groups in the incidences of tonsillectomy and appendectomy. Allergic and rheumatic diseases were nearly twice as frequent in the parents of the patients with HD than in those of the controls. (23 Refs) (In POL)

MALIGNANT LYMPHOMA: DIAGNOSIS AND STAGING

11. METABOLIC ACTIVITY OF LYMPHOMA CELLS AND CLINICAL COURSE IN NON-HODGKIN LYMPHOMA (NHL).

Monti M, Brandt L, Ikomi-Kumm J, Olsson H, Wadso I

Dept. Internal Medicine, Univ. Hosp., S-22185 Lund, Sweden

Scand J Haematol; 27(5):305-310 1981

By microcalorimetry the metabolic activity of malignant cells from 21 patients with non-Hodgkin lymphoma was monitored. Heat production, a measure of the metabolic activity of cells, showed positive correlation with the clinical course of the disease. The heat produced by tumor cells from patients with progressive disease was 5.5 pW/cell, while that from patients responding to treatment was 3.1 pW/cell. The difference between the two groups is significant (p greater than 0.05). A higher heat production was obtained in tumor cells from 7 out of 10 patients who were unresponsive to the therapy when compared with cells from 11 patients who had become asymptomatic as a result of the same therapy. Also heat production from blood lymphocytes was found to be higher (p less than 0.005) in the group of patients with progressive disease as compared to the group of patients who responded to therapy. The present results indicate an association between high heat production in lymphoma cells and blood lymphocytes and a poor prognosis. (Author abstract) (10 Refs)

12. ULTRASTRUCTURAL COMPARISON OF HODGKIN'S AND NON-HODGKIN'S LYMPHOMAS.

Peiper SC, Kahn LB

Dept. Pathology, St. Jude Children's Res. Hosp., 332 North Lauderdale, P. O. Box 318, Memphis, Tennessee, 38101

Histopathology; 6(1):93-109 1982

Ultrastructural features of Reed-Sternberg (RS) cells were compared with those of neoplastic large lymphoid cells from a variety of non-Hodgkin's lymphomas of large cell type (large cleaved and non-cleaved follicle center cells, immunoblasts, lymphoblasts) and with those of non-neoplastic macrophages, including epithelioid cells present in the lesions. The RS cell cytosol contained an abundance of organelles, frequently in a dense paranuclear location. The Golgi apparatus was hyperplastic and multiple, and glycogen and lipid droplets were frequently demonstrated in the same cell. The large lymphocytes of follicular center cell lymphomas had a sparse, non-complex population of cytoplasmic organelles, the immunoblastic lymphoma had more abundant polysomes and rough endoplasmic reticulum and a well-developed Golgi. The reactive epithelioid histiocytes also had a complex population of cytoplasmic organelles including angulated lysosomes, lipid droplets, tubular mitochondria, and cytoplasmic filopodia. Reactive histiocytes were the cells most likely to be confused with RS cells at the ultrastructural level, especially when the nucleoli were prominent. RS cells bore a closer resemblance to the reactive epithelioid histiocytes than to neoplastic large lymphoid cells. Such a finding favors the non-lymphoid origin of the RS cell. (23 Refs)

13. AN ANALYSIS OF CHROMOSOME FINDINGS IN NON-HODGKIN'S LYMPHOMAS.

Kaneko Y, Abe R, Sampi K, Sakurai M

(c/o Sakurai) Dept. Clinical Lab., Saitama Cancer Center, 818 Komuro, Ina, Saitama 362, Japan

Cancer Genet Cytogenet; 5(2):107-121 1982

Banding studies were done on tissues from tumors excised from 22 Japanese patients with non-Hodgkin's lymphomas. All tumors were found to be associated with aneuploidy. The chromosome abnormalities were diverse, with each chromosome type being involved in these abnormalities. Terminal deletions, derivative chromosomes as a result of unbalanced or non-reciprocal translocations, and markers of totally or partially unknown origin accounted for the majority of the structural abnormalities. Balanced reciprocal translocations were seen only occasionally. The 14q, 6q-, partial trisomy of 1q, 11q, 18q, and 19q abnormalities were seen in more than two patients. The incidence of a missing sex chromosome was significantly higher than that of autosomes, but no particular other karyotypic abnormality seemed to be associated with the event. All six patients whose chromosomes could be totally characterized were in complete remission. Patients with one or more markers of unknown origin (either totally or partially), had a median survival of only 8 mo (p less than 0.01). Five of the former six patients showed a nodular histology. Fifteen of the latter 16 patients had a diffuse histology, with 13 of the 15 having diffuse histiocytic lymphoma. The median survival of 9.5 mo for the 14 with only abnormal metaphases in the lymphatic tissues (AA-group) was shorter than the 26 mo for the 7 patients with both normal and abnormal metaphases (AN-group). Thus certain aspects of chromosomal changes appear to correlate with histology and/or prognosis in non-Hodgkin's lymphomas. (Author abstract) (29 Refs)

14. IMMUNOBLASTIC SARCOMA: MORPHOLOGIC CRITERIA AND THE DISTINCTION OF B AND T CELL TYPES.

Maurer R, Taylor CR, Parker JW, Cramer A, Lukes RJ
Inst. Pathology, Univ. Hosp., CH-8091 Zurich, Switzerland
Oncology; 39(1):42-50 1982

Immunologic concepts have facilitated the recognition within the histiocytic lymphoma group of the Rappaport classification of five diagnostic categories of lymphoma (follicular center cell lymphoma large cleaved and large non-cleaved types, immunoblastic sarcoma B cell type, immunoblastic sarcoma T cell type and 'true histiocytic lymphoma'). The first four of these 'large cell lymphomas' are closely related biologically and are difficult to distinguish histologically. This paper purports to examine the morphologic criteria employed in the differential diagnosis of these four large cell lymphomas in an objective manner, utilizing carefully prepared histologic sections from 24 cases of lymphoma that had been subjected to detailed B and T cell characterization by surface marker methods. Eighteen morphologic criteria were evaluated by four observers independently. The results show that reliable histologic distinctions can be made on histologic grounds in a proportion of cases only and that individual criteria show more overlap within diagnostic criteria than previously recognized. This is attributed in part to the close biologic relationship of these neoplasms. It is also recognized that the morphologic criteria are subtle and that the pathologist should have the advantage of auxiliary techniques - cytochemistry, immunohistology, surface marker techniques - to achieve reliable distinction of functional types within the diffuse histiocytic group of Rappaport. (Author abstract) (27 Refs)

15. MANTLE-ZONE LYMPHOMA: A FOLLICULAR VARIANT OF INTERMEDIATE LYMPHOCYTIC LYMPHOMA.

Weisenburger DD, Kim H, Rappaport H
Dept. Pathology, Mercy San Juan Hosp., 6501 Coyle Ave., Carmichael, CA, 95608
Cancer; 49(7):1429-1438 1982

A clinicopathologic analysis of 12 cases of a morphologically distinctive non-Hodgkin's malignant lymphoma which appeared to arise from the mantle zones of secondary lymphoid follicles is presented. In lymph node and spleen sections, atypical small lymphoid cells with slightly irregular and indented nuclear contours proliferated as wide mantles around non-neoplastic-appearing germinal centers. Surface marker analysis performed on lymph nodes revealed a monoclonal B-cell proliferation in two cases. Clinically, the patients usually had advanced disease (Stage III or IV) associated with splenomegaly. This lymphoma appears to be relatively low-grade, since 9 of 12 patients are alive with a median follow-up period of 28.5 mo. We believe that this 'mantle-zone lymphoma' represents a nodular or follicular variant of intermediate lymphocytic lymphoma. (Author abstract) (24 Refs)

16. COMPUTED TOMOGRAPHY IN LYMPHOMA. EXPERIENCE IN 500 PATIENTS.

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Nouv Rev Fr Hematol; 23(1):13-15 1981

Computed tomography (CT) findings of more than 500 patients with lymphoma were reviewed. In patients with non-Hodgkin's lymphoma scanned with clinical remission, a normal CT scan in those with diffuse pathology was associated with relapse-free survival. In those with nodular lymphoma, abnormal CT scans were not necessarily associated with relapse, and no significant different in relapse-free survival was observed between patients with normal and those with abnormal CT scans. Seventeen of 19 abnormal areas in patients who were alive and well were in the lymph nodes, compared with 6/13 areas in relapsed patients. CT may be important in Hodgkin's disease and in the diffuse histology of non-Hodgkin's lymphoma. Any investigation that indicates the presence of treatable residual disease might increase the survival rate by allowing complete treatment of patients. CT is useful in patients with non-Hodgkin's lymphoma with diffuse histology for predicting survival in patients in complete clinical remission. CT can accurately indicate residual disease with in the abdomen; 76% with abnormal scans relapsed and died or had progressive disease, while only 1/22 patients with normal CT scans relapsed. CT studies showed that most patients who relapsed should be regarded as having generalized disease. (9 Refs)

17. LIMITED CT STUDIES IN MONITORING TREATMENT OF LYMPHOMA.

Thomas JL, Barnes PA, Bernardino ME, Hagemeister FB

Dept. Diagnostic Radiology, Univ. Texas System Cancer Center, M. D. Anderson Hosp. and Tumor Inst., 6723 Bertner Ave., Houston, TX, 77030

AJR; 138(3):537-539 1982

One hundred and two follow-up CT studies in 50 patients with a diagnosis of lymphoma were reviewed to determine the efficacy of limited CT studies for determining therapy. The overall correlation between the limited CT study and the complete CT study was 98%. No mixed responses occurred in 102 cases. Two patients, both with diffuse histocytic lymphoma treated by chemotherapy, showed progression of disease outside a stable tumor bed not detected by a limited CT study. The economic implications, technique, and limitations of limited CT studies are presented. (Author abstract) (8 Refs)

18. CYTOLOGICAL DIAGNOSIS OF LYMPHOMA IN SEROUS EFFUSIONS.

Spriggs AI, Vanhegan RI

Lab. Clinical Cytology, Churchill Hosp., Headington, Oxford OX3 7LJ, England

J Clin Pathol; 34(12):1311-1325 1981

A consecutive series is presented of 100 cases of malignant lymphoma in which a correlation could be made between the histological findings and the cytology of pleural or peritoneal fluid or both. Using the Kiel classification, 80 cases could be given a histological label, while 20 remain unclassified. In those cases in which lymphoma cells were identifiable in the serous fluid, their morphology was studied and was found in general to correlate well with the cell-type expected from the histology. It is not claimed that the type of lymphoma can be reliably diagnosed from the cytology of pleural or peritoneal fluid, but an opinion can be provided as to the grade (high or low), and in some cases it is also possible to give an indication of the cell-type involved. (Author abstract) (40 Refs)

19. PRIMARY LYMPHOMA OF THE CENTRAL NERVOUS SYSTEM.

Letendre L, Banks PM, Reese DF, Miller RH, Scanlon PW, Kiely JM
Mayo Clinic, 200 First St. SW,, Rochester, MN, 55905
Cancer; 49(5):939-943 1982

Primary intracranial lymphoma usually remains localized to the central nervous system, and aggressive radiotherapy will prolong some patients' remissions and perhaps cure them. Although the lesion is usually believed to arise from histiocytes or reticulum cells, at least some of the neoplasms are of B-lymphocyte origin. Provisional diagnosis occasionally may be possible by identifying lymphoma cells in the cerebrospinal fluid by using the cytocentrifuge. The use of computed tomography of the head may decrease the need of arteriography for tumor localization. (Author abstract) (33 Refs)

20. PULMONARY LYMPHOMAS SIMULATING LYMPHOMATOID GRANULOMATOSIS.

Colby TV, Carrington CB
Dept. Pathology, Stanford Univ. Medical Center, Stanford, CA, 94305
Am J Surg Pathol; 6(1):19-32 1982

Thirty cases of malignant lymphoma with prominant vascular lesions in the lungs are described. Twenty patients (Group 1) presented with pulmonary disease and 10 patients (Group 2) had pulmonary lesions that were recognized after lymphomatous lesions had been discovered at other sites. Groups 1 and 2 were histologically indistinguishable; necrosis, vascular infiltration, and foci of a histologically polymorphous and benign infiltrate were present in both. The key to recognition of malignant lymphoma rested on careful evaluation of the cytologic features and identification of foci composed of monomorphous atypical lymphoid cells. In cases of lymphoma, infiltrates followed lymphatic routes; prognosis was poor, although two patients in Group 1 responded to steroid treatment following biopsy or resection. (18 Refs)

21. INVOLVEMENT OF THE HEART BY MALIGNANT LYMPHOMA. A CLINICOPATHOLOGIC STUDY.

McDonnell PJ, Mann RB, Bulkley BH
(c/o Bulkley), Johns Hopkins Hosp., 600 N. Wolfe St., Baltimore, MD, 21205
Cancer; 49(5):944-951 1982

Although involvement of the heart by malignant lymphoma is relatively common, it is difficult to detect antemortem, and only a small number of studies discuss this subject in the literature. The authors reviewed the 150 patients with malignant lymphoma autopsied at this hospital and studied the 13 (8.7%) who were found to have metastases to the heart or parietal pericardium. Four patients had Hodgkin's disease, and nine non-Hodgkin's lymphoma. Cardiac or pericardial disease apparently resulted from retrograde lymphatic spread, hematogenous spread, and direct extension from other intrathoracic tumor masses. In two cases, lymphomatous involvement of the heart and pericardium was the immediate cause of death; in one of these, myocardial infiltration was detected during life. For the group as a whole, the signs and symptoms of cardiac dysfunction were typically absent or nonspecific, and electrocardiograms and thallium imaging were not effective screening tools for lymphoma metastases. The findings suggest, however, that the most destructive form of cardiac involvement is that associated with direct epicardial spread, and that this form appears with cardiac dysfunction, which should clinically suggest its presence. (Author abstract) (41 Refs)

22. ENDOSCOPIC FEATURES OF PRIMARY SMALL BOWEL LYMPHOMA: A PROPOSED ENDOSCOPIC CLASSIFICATION.

Barakat MH
Gastroenterology Section, Kuwait Univ. Medical Faculty, Al-Sabah Hosp., Kuwait, Kuwait
Gut; 23(1):36-41 1982

Primary small bowel lymphoma is relatively common in Middle Eastern countries. Of 29 such cases, proximal small bowel endoscopy was positive in 26 (89.6%) and, on the basis of endoscopy alone, the diagnosis of lymphoma was confidently made in 24 patients (82.7%). The endoscopic biopsy was diagnostic in 19 of the 26 patients with visible mucosal abnormalities (73%). Four types of lesions have been seen on the basis of which an endoscopic classification is being proposed. This classification may be of therapeutic and prognostic value. (Author abstract) (25 Refs)

23. GASTROINTESTINAL LESIONS OF MALIGNANT LYMPHOMAS.

Kuyama Y, Tamaki N, Bessho H, Nakamura R, Miyasaka K, Hayashi M, Okada H, Okamoto M, Momoi H
First Dept. Internal Medicine, Tokyo Medical and Dental Univ., Tokyo, Japan
Gastroenterol Endosc; 23(2):293-299 1981

Infiltrative gastrointestinal lesions were studied in 44 patients (13-74 yr old; approx male:female ratio 2:1) with whole-body malignant lymphoma. Histologically, cases of infiltrative gastrointestinal lesions were divided based on presence of Hodgkin's or non-Hodgkin's disease; infiltrative gastrointestinal lesions were observed in 1/9 and 10/35 patients, respectively. Frequency of infiltrative gastrointestinal lesions was highest in the patients who were 40-69 yr old. Infiltrating lymphomas were observed in the stomach in six patients, small intestine in six, and large intestine in three. Gastrointestinal involvement of the malignant lymphomas was of the ulcerative type in 9/15, infiltrative type in 3/15, and tumorous type in 3/15. Benign gastrointestinal lesions such as gastric ulcers (7 cases) and small intestinal ulcers (3) were also observed. Massive hemorrhage was observed in 14/44 patients and was thought to be a primary factor in patient prognosis. One patient was followed for 3 yr; initially, a IIc-like gastric lesion was observed. Submucosal tumors and ulcerative lesions developed later, and infiltration of lymphosarcoma was diagnosed after surgical resection of the stomach. (16 Refs) (In JPN)

24. SONOGRAPHIC DEMONSTRATION OF ABDOMINAL VISCERAL LYMPH NODE ENLARGEMENT.

Ritchie WG
Dept. Radiology, Pennsylvania Hosp., 8th and Spruce St., Philadelphia, PA, 19107
AJR; 138(3):517-521 1982

Sonography technique and anatomical considerations for ultrasonography to detect abdominal visceral lymph node enlargement (LNE) are presented. Visceral LNE are frequently found in patients with Hodgkin's disease, non-hodgkin lymphomas, metastatic extension of primary tumors of the digestive tract, or metastases of extraabdominal tumors. Detection of lymphadenopathy requires knowledge of the lymphatic drainage of intraabdominal organs. Intraabdominal LNE occurs in relation to the visceral branches of the inferior vena cava and abdominal aorta. LNE at the esophagogastric junction, celiac axis, and around the inferior and superior mesenteric arteries can be detected by longitudinal parasagittal sonograms (LPS) of the aorta. LNE at the porta hepatis can be detected by LPS of the inferior vena cava. Findings of LNE should be confirmed by transverse sonograms at the appropriate levels. Transverse sonograms can also detect intrahepatic obstruction of the bile duct and LNE along the axis of the splenic and hepatic arteries. Detection of splenic LNE usually requires axial scanning in the left lateral decubitus position using the spleen as an acoustic window. Patients with suspected metastasis or lymphoma should receive LPS along the axis of the aorta and vena cava, because most LNE other than splenic LNE can be detected by these scans. Sequential sonography should be performed to determine response to therapy. (15 Refs)

25. BONE MARROW AND BLOOD INVOLVEMENT BY LYMPHOMA IN RELATIONSHIP TO THE LUKES-COLLINS CLASSIFICATION.

Foucar K, McKenna RW, Frizzera G, Brunning RD
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Cancer; 49(5):888-897 1982

The incidence, pattern, extent, and morphology of bone marrow involvement in 176 cases of non-Hodgkin's lymphoma (NHL) were studied in relationship to the Lukes-Collins classification. Ninety percent of the cases were B-cell lymphomas; 10% were T-cell lymphomas. In 53% of cases there was bone marrow involvement by lymphoma at diagnosis. Marrow involvement was most frequently found in the small lymphocyte (B), small cleaved follicular center cell (FCC), and convoluted lymphocyte lymphomas. Frequently, the extent of bone marrow biopsy replacement by lymphoma was less than 30%; the pattern of infiltration was predominantly focal (70%). Cytologic agreement between lymph node and bone marrow specimens was always present in small lymphocyte (B), small noncleaved FCC, convoluted lymphocyte, and lymphoepithelioid cell lymphomas. Cytologic diversity between lymph node and marrow was noted in 20% of small cleaved FCC, 40% (2/5) of large cleaved FCC, and 38% (3/8) of large noncleaved FCC lymphomas. In 79% of all involved cases, both bone marrow biopsy sections and aspirate smears were diagnostic of NHL; only biopsy sections were positive in 18%, and only smears were positive in 3%. The Lukes-Collins classification predicts a high incidence of bone marrow involvement for small lymphocyte (B), small cleaved FCC, and convoluted lymphocyte lymphomas. (Author abstract) (14 Refs)

26. LYMPHOPROLIFERATIVE DISEASES IN BONE MARROW.

Bartl R
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Fortschr Med; 100(3):65 1982

The diagnostic and prognostic values of bone marrow (BM) biopsies of patients with lymphoproliferative disease are examined through a summary of the results of 1,788 such procedures. BM involvement was established in 85% of 240 multiple myeloma patients, 69% of 816 patients with non-Hodgkin's lymphoma (NHL), and 14% of 732 patients with lymphogranulomatosis. It is suggested that the advantages of BM biopsy include early diagnosis, classification, and staging of multiple myeloma, accurate identification of hairy-cell leukemia, and classification of NHLs into prognostically relevant stages. (no Refs) (In GER)

27. HISTOLOGIC PROGRESSION IN NON-HODGKIN'S LYMPHOMA.

Hubbard SM, Chabner BA, DeVita VT, Simon R, Berard CW, Jones RB, Garvin AJ, Canellos GP, Osborne CK, Young RC
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Blood; 59(2):258-264 1982

We retrospectively evaluated the clinical course and biopsy specimens from 515 consecutive non-Hodgkin's lymphoma patients in an attempt to determine the clinical importance of documented changes in histology over time. Two-hundred and five of these patients had an initial diagnosis of nodular lymphoma and were reviewed for this analysis. Sixty-three underwent a repeat biopsy greater than 6 mo after initial diagnosis. In 23 patients, these repeat biopsies revealed a change in histology to a diffuse pattern and/or a change to a larger 'histiocytic' cell type, while repeat biopsies for the other 40 (63%) disclosed persistence of a nodular pattern and no clear change in basic cell type. Progression from nodular lymphoma to diffuse histiocytic, mixed, or undifferentiated types of lymphomas of Rappaport was found in repeat biopsies obtained from 19 patients (30%). Prognosis for survival following a biopsy that demonstrated histologic change was related to the histology demonstrated at the most recent biopsy and to the response to subsequent drug treatment. Survival following repeat biopsy for these 19 patients was significantly shorter than for the 40 patients whose histology remained nodular (p less than 0.001). However, attainment of a complete remission with intensive combination chemotherapy was associated with prolonged disease-free survival in one patient. Since prior treatment may compromise the ability to achieve a complete response to chemotherapy in patients with nodular lymphoma who develop an aggressive diffuse histology, the likelihood of histologic progression must be considered in the design of future clinical trials in nodular lymphoma. Histologic progression, while associated with a worsened prognosis, does not preclude attainment of a complete response to intensive chemotherapy. (Author abstract) (34 Refs)

28. REGRESSING ATYPICAL HISTIOCYTOSIS: A CUTANEOUS PROLIFERATION OF ATYPICAL NEOPLASTIC HISTIOCYTES WITH UNEXPECTEDLY INDOLENT BIOLOGIC BEHAVIOR.

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Cancer; 49(5):959-970 1982

Regressing atypical histiocytosis (RAH) of skin is a cutaneous noduloulcerative proliferation of atypical neoplastic histiocytes with concomitant polymorphous inflammation, frequently pronounced epidermal hyperplasia, and an unexpectedly indolent biologic course. Spontaneous regression and recurrence without systemic spread were the course in follow-up periods of over 6 yr. Histopathologically, characteristic-appearing atypical mononuclear and multinucleated 'RAH' cells showed erythrophagocytosis as well as ultrastructural, surface marker, and enzyme cytochemical features indicating histiocytic differentiation. Cytogenetic analysis showed aneuploidy and several marker chromosomes including 14q. Its benign biologic course clearly distinguished this entity from malignant histiocytosis, large cell lymphoma, and Hodgkin's disease. The histiocytic atypical cells further distinguished it from the T-cell lesions of the skin, such as mycosis fungoides and lymphomatoid papulosis. This entity is readily confused with malignant lymphoreticular disease, melanoma, or squamous carcinoma. (Author abstract) (68 Refs)

29. ELECTRON MICROSCOPIC IDENTIFICATION OF LANGERHANS CELLS IN THE DERMAL INFILTRATES OF MYCOSIS FUNGOIDES.

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J Invest Dermatol; 78(2):102-107 1982

The importance of the physical interaction between epidermal Langerhans cells and malignant cells in mycosis fungoides (MF) has been stressed recently. To further evaluate the concept, electron microscopic study was carried out to identify whether or not Langerhans cells are also present in the dermal infiltrates of MF. The cells with characteristic Langerhans cell-granules were found in the dermal infiltrates, from early patch to tumor lesions of MF. No vacuolous change suggestive of cell degeneration was found in these cells. These Langerhans cells revealed only a small number of specific granules and nuclear cleavage and chromatin pattern similar to those of malignant lymphoid cells, thus hardly differentiating two cell types in a low power view. Similar to epidermal MF lesions, however, a close apposition of dermal Langerhans cells with malignant lymphoid cells was seen. On one occasion, one Langerhans cell was present at the epidermodermal junction, appearing as being in the process of crossing over the basal lamina. Inasmuch as malignant cells in MF have been shown to possess the functional properties of helper T cells and receptors for Ia (immune associated antigen), expressed in the epidermis solely on Langerhans cells, our findings may further suggest that these malignant T cells bind to Langerhans cells through a 'lock and Key' mechanism involving membrane-bound Ia. (Author abstract) (23 Refs)

30. AN ULTRASTRUCTURAL STUDY OF THE MONONUCLEAR CELL INFILTRATE OF MYCOSIS FUNGOIDES AND POIKILODERMA ATROPHICANS VASCULARE.

Chu AC, Morgan EW, MacDonald DM
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Clin Exp Dermatol; 7(1):11-19 1982

Skin biopsies from patients with pre-mycotic eruptions and plaque and tumid mycosis fungoides (MF) were examined by electron microscopy to assess the value of the presence of abnormal lymphoid cells in early diagnosis of MF. In 21/25 specimens from patients with untreated MF and in all 3 from patients with poikiloderma atrophicans vasculare, mononuclear cells infiltrated the epidermis. In all dermal filtrates examined, abnormal lymphoid cells were conspicuous; the cells possessed irregular nuclear outlines ranging from mild indentation to grossly cerebriform shapes. In the dermis, lymphoid cells comprising 30-60% of the infiltrate were seen in a mixed cellular infiltrate composed of normal mature lymphocytes, histiocytes, mast cells, eosinophils, and occasional polymorphonuclear WBC and plasma cells. Lymphoblasts were identified in dermal infiltrates of two patients with tumid MF. Bizarre histiocytic cells resembling the interdigitating reticulum cell of lymph node T cell areas were observed. In epidermal infiltrate, abnormal lymphoid cells infiltrates singly between keratinocytes and less frequently in groups, forming Pautrier microabscesses. Langerhans cells were observed only in the epidermis, usually isolated but occasionally in contact with lymphoid cells. The diagnostic importance of ultrastructural findings in MF is affirmed. (27 Refs)

MALIGNANT LYMPHOMA: CLINICAL IMMUNOLOGY AND IMMUNOTHERAPY

31. THE RELATIONSHIP BETWEEN T LYMPHOCYTE SUBSETS AND IA-LIKE ANTIGEN POSITIVE NONLYMPHOID CELLS IN EARLY STAGES OF CUTANEOUS T CELL LYMPHOMA.

Thomas JA, Janossy G, Path MR, Graham-Brown RA, Kung PC, Goldstein G
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J Invest Dermatol; 78(2):169-176 1982

Immunofluorescence studies were carried out in cutaneous T cell lymphoma (mycosis fungoides) in order to analyze the microanatomical relationship of the different T lymphocyte subsets (inducer and suppressor/cytotoxic cell populations) to large nonlymphoid Langerhans-type and so-called 'indeterminate' or interdigitating cells. The conventional and mouse (monoclonal) antibodies were used in various combinations using fluorescein and rhodamine labeled second layers. In five of the seven cases studied the dermal infiltrate consisted of numerous T (HuTLA) lymphocytes, 80-90% of which expressed the inducer phenotype (HuTLA,OKT4). Most of these cells formed close contact with large cells exhibiting large amounts of Ia-like antigens. These cells corresponded to the interdigitating and indeterminate cells in the sections. By contrast, only small numbers (10-20%) of T cells of suppressor/cytotoxic type (HuTLA,OKT8) were seen. These did not show a close affinity to the Ia-like antigen positive nonlymphoid component but appeared to have a predilection for the epidermis. Epidermal Langerhans cells, also strongly Ia-like antigen positive, were further defined by two monoclonal antibodies reacting with a cortical thymocyte antigen HTA-1. Although Langerhans cells are probably related to the Ia-like antigen positive dermal cells only a few of the abundant latter population were HTA-1. In the remaining two cases, larger populations of OKT8 (suppressor/cytotoxic) cells were seen and could be heralding a particularly benign course. These observations indicate a close functional relationship between the lymphoid and Ia-like antigen positive dermal cells during the pre-malignant phase of cutaneous T cell lymphoma. (Author abstract) (39 Refs)

MALIGNANT LYMPHOMA: CHEMOTHERAPY

32. A PILOT STUDY OF HIGH-DOSE 1-BETA-D-ARABINOFURANOSYLCYTOSINE FOR ACUTE LEUKEMIA AND REFRACTORY LYMPHOMA: CLINICAL RESPONSE AND PHARMACOLOGY.

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Dept. Medical Oncology, Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY, 14263
Cancer Res; 42(4):1587-1594 1982

The chemical 1-beta-D-arabinofuranosylcytosine (ara-C), 2 or 3 g/sq m, was administered as a 1-hr iv infusion every 12 hr for 10 or 12 doses to patients with acute leukemia and refractory lymphoma. Four of seven patients with relapsed or refractory acute myelocytic leukemia and two of four patients with previously untreated acute myelocytic leukemia achieved complete remission. Of five treatment failures, two patients had leukemia which was clearly resistant to high-dose ara-C, and three patients died of infections or hemorrhagic complications during periods of pancytopenia. Three patients with acute myelocytic leukemia in remission received high-dose ara-C as consolidation therapy following previous courses of intensive, multiagent consolidation chemotherapy. Two of these three patients had prolonged thrombocytopenia following high-dose ara-C. Five patients with refractory acute lymphocytic leukemia were treated. Three patients achieved partial remission, and two patients had drug-resistant disease. Complete or partial disappearance of measurable disease parameters was seen in three of three patients with refractory lymphoma. Response was seen in five of five patients with meningeal leukemia, including complete response in one patient with extensive meningeal infiltration. Toxicity of this regimen was generally moderate and limited to pancytopenia and mild nausea. Patients who had received prior multiagent consolidation chemotherapy appeared to be at greater risk for hematopoietic toxicity. Patients who had received prior cranial irradiation or intrathecal chemotherapy appeared to be at greater risk for neurological toxicity. Plasma levels of ara-C immediately after completion of the infusion were 17.96 -8.02 (SD) and 35.0 -2.8 ug/ml for doses of 2 and 3 g/sq m, respectively. From 160 to 720 min following completion of the infusion, the plasma levels of drug were comparable to steady-state levels achieved with a continuous infusion of ara-C at 100 mg/sq m over 24 hr. A high degree of penetration into the central nervous system was demonstrated. High-dose ara-C has substantial activity against leukemic and lymphomatous cell populations, including cell populations resistant to conventional doses of the drug, and is an effective treatment modality for patients with these diseases. The high degree of penetration into the central nervous system suggests that this drug regimen may be useful as consolidation therapy for patients at high risk for central nervous system disease. (Author abstract) (23 Refs)

33. METHOTREXATE AS A SINGLE AGENT AND IN COMBINATION CHEMOTHERAPY FOR THE TREATMENT OF NON-HODGKIN'S LYMPHOMA OF UNFAVORABLE HISTOLOGY.

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Cancer Treat Rep; 65(Suppl1):125-129 1981

High-dose methotrexate (HDMTX) with citrovorum factor (CF) was used to treat non-Hodgkin's lymphomas either as a single agent in those patients who had previously failed to respond to conventional chemotherapy or in previously untreated patients in combination with bleomycin, Adriamycin, cytoxan, and vincristine. Twenty-five patients who had been previously treated and were refractory to cytotoxic chemotherapy were treated with HDMTX ranging between 1 and 7.5 g/m2 as an iv infusion over 20-40 min. CF rescue was begun at 24 hr and was maintained orally every 6 hr at 10 mg/m2 for a total of 72 hr. In instances where the 24-hr serum level of MTX was in excess of 1 X 10-7M, the dose of CF was increased to 100 mg/m2 every 3 hr until the serum MTX level fell into the appropriate range. Of the 25 patients, 13 (52%) responded. Response duration was brief, lasting a median of 2 mo. Three patients had prolonged control lasting 13, 16 and 21 mo respectively. Five of the six patients with central nervous system (CNS) involvement have demonstrated marked clearing of spinal fluid abnormalities and reversion of brain scans toward normal. Fifty-four previously untreated patients with diffuse histiocytic or undifferentiated lymphoma have been treated with combination chemotherapy including MTX given at the level of 3 g/m2 on Day 14 of a cycle. Bleomycin, Adriamycin, cyclophosphamide, and vincristine are given on Day 1 of the cycle. Dexamethasone 6 mg/m2 is given orally on Days 1 through 5. The cycle is repeated on Day 21, and patients are treated with 10 such cycles for a total of 30 wk. Of our 42 patients who are evaluable for response and who have completed chemotherapy, 33 (78%) achieved a complete remission (CR). A total of seven patients have relapsed. Only one patient in the CR group has relapsed in the CNS after the cessation of chemotherapy. (Author abstract) (19 Refs)

34. CYCLOPHOSPHAMIDE, DOXORUBICIN, VINCRISTINE, AND LOW-DOSE CONTINUOUS INFUSION BLEOMYCIN IN NON-HODGKIN'S LYMPHOMA: CANCER AND LEUKEMIA GROUP B STUDY 7804.

Ginsberg SJ, Crooke ST, Bloomfield CD, Peterson B, Kennedy BJ, Blom J, Ellison RR, Pajak TF, Gottlieb AJ
Dept. Medicine, SUNY-Upstate Medical Center, 750 East Adams St., Syracuse, NY, 13210
Cancer; 49(7):1346-1352 1982

Fifty-eight evaluable patients with non-Hodgkin's lymphoma were treated with a low dose, 120-hr continuous iv infusion of bleomycin in combination with cyclophosphamide, doxorubicin, vincristine, and prednisone. Pharmacokinetic data, obtained in six patients, confirm that steady-state plasma concentrations of bleomycin can be attained even with the administration of 2 units/day of the drug. Neither clinical pulmonary toxicity nor subclinical pulmonary changes, as determined by serial measurement of the single breath carbon monoxide-diffusing capacity, were observed. Compared to similar chemotherapeutic programs utilizing bolus administration of bleomycin, pulmonary toxicity may be reduced. Response frequencies among 37 previously untreated patients were similar to those obtained using the same chemotherapeutic agents but with iv bolus administration of bleomycin. In addition, 18 of 21 patients who had received prior chemotherapy responded. Low dose, continuous iv infusion of bleomycin may improve the therapeutic index of combination chemotherapy programs for non-Hodgkin's lymphoma. (Author abstract) (19 Refs)

35. EVALUATION OF TWO COMBINATION CHEMOTHERAPIES IN PREVIOUSLY UNTREATED NON HODGKIN'S LYMPHOMA.

Somoza N, Pavlovsky S, Suarez A, Morgenfeld M, Besuschio SC, Bezares R, Quiroga Micheo E, Lein NJ, De Maria H
Instituto Municipal de Hematologia, Hospital Ramos Mejia, Buenos Aires, Argentina
Medicina (B Aires); 41(Suppl):35-43 1981

Patients with previously untreated, histologically confirmed non-Hodgkin's lymphoma (NHL) were treated either with a regimen consisting of cyclophosphamide (CPM), vincristine (VCR), procarbazine, prednisone (PRN), and lomustine (COPP-CCNU) or with a regimen consisting of CPM, daunomycin, VCR, and PRN (C-DOP). After induction therapy the patients underwent complete restaging. Patients in complete remission (RE) received maintainance therapy with chlorambucil for 20 days every mo for a period of 2 yr. Patients in partial RE received two extra cycles of the same therapy and then restaging. Complete RE was achieved in 37/74 patients receiving C-DOP, partial remission in 18/74, no response in 12/74, and 7/74 died. Results obtained in patients receiving COPP-CCNU were 53/83, 13/83, 6/83, and 11/83, respectively. After 48 mo, 47% of COPP-CCNU patients and 41% of C-DOP patients remained in complete RE. Five yr after diagnosis, 42% of COPP-CCNU patients and 32% of C-DOP patients were alive. No relationship between survival and histologic type or staging was noted. Both polychemotherapies gave similar results for induction, duration of RE, and survival. (13 Refs)

36. COMBINATION CHEMOTHERAPY OF UNFAVOURABLE PROGNOSIS NON-HODGKIN'S LYMPHOMA (NHL). A RETROSPECTIVE STUDY OF 53 CASES.

Mandelli F, Biagini C, Baroni CD, Bosman C, Allmena G, Anselmo AP, De Luca AM, Maurizi Enrici R, Petti N, Amadori S, Papa G
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Haematologica (Pavia); 66(6):740-749 1981

Fifty three patients with unfavorable prognosis of non-Hodgkin's lymphoma treated with an acute leukemia type combination chemotherapy were studied retrospectively. Parameters taken into consideration were age (less than 15 yr old, 11 patients), extensive mediastinal involvement (5 patients), Stage III and IV diffuse histology (22 patients), and patients relapsed or not responsive to polychemotherapy (previous treatment, 15 patients). Median age of all patients (35 males, 18 females, 3-70 yr old), was 28 yr. Chemotherapy included combinations of adriamycine, vincristine, cyclophosphamide, prednisone, and cytosine arabinoside. Results showed that complete remission was reached in 100% of patients less than 15 yr old, 3/5 with massive mediastinal involvement, 11/22 with Stage III and IV, and in 3/15 patients relapsed or resistant to previous treatment. The median survival rate appeared directly related to the remission rate, lasting 2 yr in 50% of the patients. The relapse rate was low during the first yr, with no difference between sub-groups. Remission rate according to the primary site of disease was 9/14 patients with lymph nodes primarily involved, 84% of the patients surviving 48 mo. Complete remission was achieved in 57% of the patients with poorly differentiated lymphocytic lymphoma, and they had a median survival of 15 mo. A serious myelodepression appeared in all patients from day 8 to day 12 after completion of each cycle of therapy. Only in 11 patients was the treatment delayed because of cytopenia. None of the patients died during the induction phase. (21 Refs)

37. THE LONG-TERM OUTLOOK FOR CHILDREN TREATED FOR NON-HODGKIN LYMPHOMAS. A REPORT OF THE CHILDREN'S SOLID TUMOR GROUP.

Goldman A, Barrett A, Bloom HJ, Graham-Pole J, Lawson DN, McElwain TJ, Malpas JS, Pritchard J, Sandland R
St. Bartholomew's Hosp., Smithfield, London EC1, England
Br J Cancer; 44(6):872-878 1981

Twenty-nine children with non-Hodgkin's lymphomas (NHL) were treated between 1974 and 1977 with a protocol based on those used for childhood ALL. Seventy-six per cent of patients had advanced disease by Ann Arbor criteria. All tumors had Rappaport's diffuse histology. Nineteen patients (65%) achieved complete remission, 14 (65%) remained alive and disease free beyond 42 mo from diagnosis. Ten patients failed to enter complete remission, of whom all died. Seven patients relapsed; five died, two remain disease free and off treatment in 19 and 29 mo. Comparison with a historic group of 20 consecutively treated children shows improved survival (p less than 0.01). Eighteen controls died. Histology was reviewed using the Kiel classification and staging according to Murphy's criteria. These are compared with the methods used initially. The improved outlook for children with NHL using intensive multiple drug regimes and cranial prophylaxis is confirmed. In staging childhood NHL, Murphy's criteria, which take into account the natural history of the disease, have greater prognostic value. Histology and pattern of outcome of the disease suggest basic differences between primary abdominal and primary mediastinal and nodal disease. This is now being confirmed with immunological typing and will be reflected in the development of future protocols. (Author abstract) (8 Refs)

38. DEFERRAL OF INITIAL THERAPY FOR ADVANCED INDOLENT LYMPHOMAS.

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Cancer Treat Rep; 66(3):417-419 1982

Management of advanced indolent lymphomas is reviewed. No curative therapy has been developed. Studies of various chemotherapy and combined therapy regimens show continuous relapses as late as 6 yr after treatment. The object of therapy, therefore, is to achieve complete response with the longest possible duration. Many patients with Stage III or IV lymphomas are symptomatically well. Lymphoma frequently progresses very slowly and may show fluctuations. Withholding therapy initially may be indicated. Advantages of withholding therapy include the possibility of a prolonged treatment-free interval, avoidance of selection of therapy-resistant tumor cells, possibility of spontaneous regression, the opportunity to initiate therapy later as needed, and the possibility that the disease may evolve spontaneously to a more aggressive and more curable form. A retrospective study indicates that survival times are not significantly different for patients receiving therapy initially and those having therapy withheld. The treatment-free interval is 10 mo for nodular mixed lymphoma, 55 mo for nodular lymphocytic, poorly differentiated lymphoma (NLPD), and 73 mo for diffuse lymphocytic, well differentiated lymphoma (DLWD). Hazards of withholding therapy include undetected disease progression, psychological burdens, and compromise of response to therapy by advanced stage of disease. Withholding therapy is a reasonable choice, particularly for patients with DLWD or NLPD. Single alkylating-agent therapy as conservative therapy is suggested when treatment is required. (11 Refs)

MALIGNANT LYMPHOMA: SURGERY

39. THE ROLE OF SURGERY IN THE MANAGEMENT OF GASTRIC LYMPHOMA.

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Cancer; 49(6):1135-1141 1982

With the development of more effective combination chemotherapy and radiation, the role of surgical resection in the management of gastric lymphoma is reappraised. A retrospective review of 32 patients with gastric lymphoma, diagnosed and treated during the period between 1966-1979, is presented in an attempt to evaluate the relative effectiveness of the various modalities of diagnosis and treatment. Preoperative gastric barium x-ray studies were abnormal in 28 patients but were infrequently diagnostic of lymphoma. Endoscopy was employed in 15 patients with washings and biopsy. the biopsies were reported: four nondiagnostic; three suspicious of tumor; three carcinomas; and in only five patients was a clear diagnosis of lymphoma established. Fifteen patients were treated on the basis of biopsy via gastroscopy, or were explored and not resected and were treated with chemotherapy and/or radiation therapy. Fourteen of the nonresected patients have died with disease; 1 patient is surviving with disease at 20 mo. Surgical resection was accomplished in 17 of the 32 cases, with 7 patients (41%) surviving from 2-12 yr. Aggressive primary chemotherapy with four-drug combination (CAOP) without surgical resection has resulted in massive upper gastrointestinal hemorrhage in four of five patients thus treated. This required emergency surgery for patients with depressed leukocyte and platelet counts. No perforation of the stomach was seen with primary chemotherapy as reported by other authors. In this series surgical exploration was necessary to establish a definite histologic diagnosis in 27 of the 32 patients. Exploration was an essential step in establishing the extent of disease to plan therapy. The only long-term survivors free of tumor were those which had been surgically resected. Resection of the gastric lymphoma prevented the complication of hemorrhage and perforation associated with chemotherapy and radiation therapy. (Author abstract) (25 Refs)

MALIGNANT LYMPHOMA: MULTIMODAL THERAPY

40. ROLE OF COMBINED-MODALITY THERAPY IN THE CURATIVE MANAGEMENT OF ADVANCED-STAGE 'FAVORABLE' NON-HODGKIN'S LYMPHOMAS.

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Cancer Treat Rep; 66(3):421-425 1982

Management of advanced stages of 'favorable' non-Hodgkin's lymphomas (NHL) is reviewed. NHL is characterized primarily by involvement of lymph nodes. Wide-field, high-dose radiotherapy (RT) has produced modest improvement in NHL. Some studies indicate that diffuse histiocytic lymphoma (DHL) in advanced stages can frequently be cured by combination chemotherapy (CCT). The 'favorable' types of NHL, nodular lymphocytic, poorly differentiated (NLPD), nodular mixed (NM), and diffuse lymphocytic, well differentiated (DLWD), show poor curability by available therapies. Current modes of treatment include initially deferred treatment, single-agent chemotherapy, (SACT), conventional high-dose RT, total-body RT (TBI), and combined modality therapy (CMT). Data for comparison of modalities is incomplete, preventing conclusive statements of effectiveness. Initially deferred treatment assumes that 'favorable' NHL is incurable by available methods. Differences in response rates and overall survival using SACT and CCT are not clear. RT is limited by the usual requirement of prolonged treatment of bulky lymph node areas and the possibility of disease progression in unirradiated areas. Two studies indicate that high-dose, total lymphoid irradiation may be effective against Stage III nodular lymphoma. TBI apparently is of only palliative value. CMT may provide the best chance of curative treatment of 'favorable' NHL, since CCT and RT are not cross-reactive, and since recurrences after RT follow different patterns from those after CCT. Induction of complete CCT, followed by RT and then more CCT is suggested. (21 Refs)

MALIGNANT LYMPHOMA: CASE REPORTS

41. TREATMENT OF B-CELL LYMPHOMA WITH MONOCLONAL ANTI-IDIOTYPE ANTIBODY.

Miller RA, Maloney DG, Warnke R, Levy R
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N Engl J Med; 306(9):517-522 1982

A 67-yr-old man with nodular, poorly differentiated, lymphocytic malignant lymphoma was treated with monoclonal anti-idiotype antibody. Partial responses were produced with leukocyte interferon and chemotherapy (cyclophosphamide, vincristine, and prednisone). Progressive lymphoma refractive to chemotherapy was shown by biopsy to be diffuse, poorly differentiated lymphocytic lymphoma. Anti-idiotype antibody (4D6) was given in a continuous 6-hr infusion. Plasmapheresis did not reduce the idiotype level. With 15 mg anti-idiotype antibody, a dramatic decrease in the idiotype level was noted. No toxicity or side effects were observed. Doses of 40 and 75 mg caused progressively greater decreases in serum idiotype; after 150 mg idiotype levels remained undetectable. The detectability of anti-idiotype coincided with the disappearance of serum idiotype. No measurable tumor response was noted after five doses of anti-idiotype; however, anti-idiotype penetrated and bound to cells within the lymph node. The patient's condition improved following four injections of 4D6, measurable tumor response occurred after the 75-mg dose, and over the next 3 wk the patient's enlarged lymph nodes gradually became smaller. The liver and spleen returned to normal size, tumors on the scalp disappeared, and platelet count and Hb rose to normal levels. Treatment was discontinued after a total of eight doses of antibody over 4 wk. The patient has remained in remission without further therapy for greater than 6 mo. (20 Refs)

42. CENTRAL NERVOUS SYSTEM LYMPHOMA PRESENTING AS DYSPHAGIA.

Benjamin SB, Eisold J, Gerhardt DC, Castell DO
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Dig Dis Sci; 27(2):155-160 1982

Two patients are presented having lymphomatous involvement of the central nervous system in whom dysphagia was the predominant symptom. All indicated studies failed to reveal evidence of direct esophageal involvement, and the dysphagia improved during treatment of the neural component. Esophageal manometric studies revealed abnormalities of the striated muscle portion of the esophagus. These two case histories suggest that invasion of the central nervous system with lymphoma may produce abnormalities of the neuromuscular control of esophageal function resulting in dysphagia. (Author abstract) (10 Refs)

43. ACQUIRED EXTRINSIC PULMONIC STENOSIS CAUSED BY MEDIASTINAL TUMORS.

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Cancer; 49(7):1496-1499 1982

Clinically detectable pulmonic stenosis resulting from compression of the pulmonary artery or right ventricular outflow tract by mediastinal tumors is uncommon. This report describes the occurrence of pulmonic stenosis secondary to a mediastinal tumor in a patient with Hodgkin's disease and in two patients with non-Hodgkin's lymphomas. Review of 35 published reports reveals that teratomas (10 cases) and Hodgkin's disease (8 cases) are the neoplasms most frequently reported to cause extrinsic pulmonic stenosis. Chest pain and dyspnea were the symptoms most commonly reported, and a pulmonic ejection murmur was the most common physical finding in patients with acquired pulmonic stenosis. The prognostic significance of acquired pulmonic stenosis secondary to mediastinal tumors is unclear. (Author abstract) (19 Refs)

44. MALIGNANT LYMPHOMA OF SMALL CLEAVED LYMPHOCYTES OF THE FOLLICULAR MANTLE ZONE.

Palutke M, Eisenberg L, Mirchandani I, Tabaczka P, Husain M
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Blood; 59(2):317-322 1982

We describe a highly unusual lymphocytic lymphoma. It appeared to originate in the mantle zones of hyperplastic follicles that had large reactive centers. The tumor cells in the mantle zone were small lymphocytes with cleaved or very irregular nuclei. They had coarse and abundant IgM, kappa surface immunoglobulin markers, and receptors for complement. The tumor involvement was generalized at the time of discovery. The diagnosis of a malignant lymphoma was initially made with difficulty because of the presence of reactive follicular centers as well as a polyclonal hypergammaglobulinemia and large numbers of interfollicular plasma cells and plasmacytoid lymphocytes containing all classes of immunoglobulin. However, 2 yr later, the follicular centers were replaced by tumor nodules composed of lymphocytes identical in appearance and immunologic type to those seen originally. This case illustrates that not all nodular lymphomas are follicular center cell (FCC) neoplasms and that morphological transformation from small round to small cleaved lymphocytes and a corresponding increase in surface immunoglobulins may take place in the follicular mantle zone. The patient had a high titer of antibody to Epstein-Barr virus (EBV) and a poor lymphocyte response to concanavalin A, but neither the tumor cells nor the plasmacytoid lymphocytes contained EBV DNA. (Author abstract) (10 Refs)

45. LYMPHOMATOID GRANULOMATOSIS. CLINICOPATHOLOGIC STUDY OF FOUR CASES AND LITERATURE REVIEW.

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(c/o Lynch) Pulmonary Div., Univ. Michigan Hosp., 1405 E. Ann St., Ann Arbor, MI, 48109
Medicine (Baltimore); 61(1):1-12 1982

Lymphomatoid granulomatosis (LYG) is a poorly understood inflammatory angitis of uncertain pathogenesis with histological similarities to Wegener's granulomatosis (WG) and atypical lymphoma. Pulmonary, constitutional, cutaneous, and central nervous system manifestations predominate, but clinical signs are extraordinarily diverse. Clinical, roentgenographic, and laboratory abnormalities are nonspecific and the diagnosis is frequently missed or delayed. We describe four cases of LYG and review the previous literature with emphasis on clinical and histological features, course, and therapy. The histological characteristics of LYG are described, and compared and contrasted with WG and atypical lymphoma. In addition to reviewing typical clinical features, we report rare findings noted in two of our cases, eg, retroperitoneal fibrosis and lytic and blastic bone lesions which expand the spectrum of the disorder and emphasize its protean nature. Our four cases reconfirm the frequency of diagnostic delay, high mortality, and poor responsiveness to therapy. In the review of our cases and previously published data, no therapeutic regimen consistently altered the course of the disease. The efficacy of corticosteroids, immunosuppressive and cytotoxic agents remains uncertain due to variable drug and dosage schedules, lack of comparable patient populations, and retrospective nature of previous reports. However, it appears that corticosteroids may transiently alter manifestations of LYG, but do not prevent ultimate progression. Cyclophosphamide may have contributed to arrest of the disease in our Cases 3 and 4, as well as in sporadic cases from the literature, but its overall efficacy appears to be limited. Multiple-agent chemotherapy has been associated with occasional responses, but generally has been unsuccessful. Surgery and radiation therapy may be helpful in selected patients with localized disease. The role of corticosteroids, cytotoxic agents, and radiation therapy, alone or in combination, needs to be clarified by prospective cooperative trials. (Author abstract) (28 Refs)

MALIGNANT LYMPHOMA: SELECTED PRE-CLINICAL STUDIES

46. IN VITRO GLUCOCORTICOID STUDIES IN HUMAN LYMPHOMA: CLINICAL AND BIOLOGIC SIGNIFICANCE.

Bloomfield CD, Smith KA, Peterson BA, Gajl-Peczalska KJ, Munck AU

Univ. Minnesota Hospitals, Box 277, Minneapolis, MN, 55455

J Steroid Biochem; 15:275-284 1981

Results from summarized studies of receptor levels from tumor cells from different tissues, in vitro glucocorticoid (GC) assays in control lymph nodes and in lymphoma, in vitro GC assays and response to GC therapy, effect of in vivo GC administration on receptor levels, and sequential studies of tumor receptors at diagnosis and relapse, on patients and volunteers, are presented. Receptor levels in tumor cells from different sites did not correlate well and since sufficient numbers of lymphoma cells (LC) from marrow and blood are available in less than 25% of patients, LC from lymph nodes were used. Median number of GC receptor sites/cell were 691 for cytoplasmic receptors, 1,481 for nodular, and 2,085 for total receptors. Inhibition of leucine incorporation by dexamethasone (DM) was significantly greater in lymphomas than in control lymph nodes. Significant differences between responders and nonresponders were not seen in DM inhibition of radiolabeled leucine or thymidine incorporation. No pretreatment clinical characteristics could be used to predict those patients who would respond to GC therapy. The fall in receptor numbers following GC administration could be explained as intrinsic regulation by the cell of receptors in response to in vivo changes in hormone (GC) level (down regulation). Data suggest that following relapse, cases initially sensitive to GC may develop resistance by selection of cells with fewer receptors, and administration of DM to patients may result in selection of lymphoma cells with lower number of receptors. Chemotherapy in addition to GC may accelerate the process. (27 Refs)

MALIGNANT LYMPHOMA: REVIEWS

47. PRIMARY GASTROINTESTINAL LYMPHOMA: A 30-YEAR REVIEW.

Weingrad DN, DeCosse JJ, Sherlock P, Straus D, Lieberman PH, Filippa DA
(c/o DeCosse), Memorial Hosp., 1275 York Ave., New York, NY, 10021
Cancer; 49(6):1258-1265 1982

The authors reviewed all cases of non-Hodgkin's lymphoma primarily involving the gastrointestinal tract treated at Memorial Hospital during the period from 1949-1978. Complete clinical records were available in 104 cases. Slides of original pathology specimens were available in 81 cases. Tumors were classified by Rappaport, Lukes-Collins and modified Kiel classifications. All patients were staged retrospectively, using modified Ann Arbor staging. The primary tumor was in the stomach in 76 patients, in the small bowel in 15 and in the large bowel in 13. The life-table survival for all patients at 5 years was 44% and for the 81 Stage I and II patients it was 53%. We found a trend toward improved survival for patients treated in the last decade ($p = 0.05$). Using Cox regression analysis, survival was found to be correlated with stage (p less than 0.0001) and involvement of adjacent structures ($p = 0.007$). For Stage I patients, resection and radiation therapy were equally effective alone in controlling local tumor even though factors responsible for the selection of either treatment could not be identified. For Stage II patients, resection combined with radiation therapy controlled local disease better than either treatment alone. For Stage II, patient survival was correlated with the pattern of nodal involvement (p less than 0.0001). Neither the choice of treatment (resection, radiation therapy, or resection with radiation therapy; $p = 0.17$) nor the involvement of resected margins ($p = 0.22$) affected survival. Among 81 Stage I and II patients, 68% had recurrences outside the primary field of treatment and 60% outside the abdomen. Systemic multiple modality therapy should be considered for patients at high risk for recurrence. (Author abstract) (27 Refs)

48. OCULAR ADNEXAL LYMPHOID NEOPLASMS: CLINICAL, HISTOPATHOLOGIC, ELECTRON MICROSCOPIC, AND IMMUNOLOGIC CHARACTERISTICS.

Knowles DM, Jakobiec FA
Lab. Surgical Pathology, Columbia Univ. Coll. Physicians and Surgeons, 630 W 168th St., New York, NY, 10032
Hum Pathol; 13(2):148-162 1982

Clinicopathologic analysis of 400 ocular adnexal lymphoid neoplasms has demonstrated that the orbital lymphoid neoplasms occur primarily in the 6th and 7th decades of life; that their benignancy or malignancy is generally indistinguishable clinically; that the orbital malignant lymphomas are most commonly small cell lymphomas; that the orbital 'histiocytic' lymphomas almost always represent an anomalous deposit of disseminated lymphoma; and that the percentage of patients with orbital lymphoma who develop systemic disease varies with the histopathology: two thirds of cases of poorly differentiated lymphocytic lymphomas, as defined cytomorphologically, have associated systemic disease. Prospective correlative clinicopathologic and immunologic analysis of 25 cases has shown that cell marker analysis divides the ocular adnexal lymphoid infiltrates into immunologically polyclonal proliferations, which show diverse but benign histopathologic features, and immunologically monoclonal B cell proliferations, which have the histologic features of malignant lymphomas. The benign, polyclonal ocular pseudolymphomas recapitulate the cell marker profile of a benign reactive lymph node with similar variations in the T cell:B cell ratio. The ocular adnexal and nodal B cell lymphomas are analogous in that they most commonly express surface IgM heavy chains and kappa light chains, express Ia antigens in parallel with SIg, and occasionally contain neoplastic B cells at various developmental stages - ie, IaSIg and IaSIg-. Correlative immunologic and ultrastructural studies have demonstrated that electron microscopy is a reliable and reproducible technique for indirectly assessing the mono- or polyclonality of an ocular adnexal lymphoid neoplasm. This study is focused on the use of hybridoma-derived monoclonal antibodies, which are capable of detecting maturational stages of B and T cell differentiation and functionally distinct T cell subsets, in order to investigate the interactional and immunoregulatory defects that participate in the generation of the ocular adnexal lymphoid proliferations. (Author abstract) (56 Refs)

49. LYMPHOMA.

Crowther D

Cancer Res. Campaign, Christie Hosp. and Holt Radium Inst., Wilmslow Road, Manchester M20 9BX, England

Cancer Chemotherapy 1981- The EORTC Cancer Chemotherapy Annual 3. Pinedo HM, ed. Amsterdam, Excerpta Medica, 504 pp, 1981.

Literature published in 1980 on the management of lymphoma is reviewed. Treatment of Hodgkin's disease in adults and children is described and salvage chemotherapy discussed. Treatment of non-Hodgkin's lymphoma is reviewed with respect to generalized lymphomas of high-grade pathology, lymphoblastic lymphoma, cutaneous T-cell lymphoma, Burkitt's lymphoma, malignant histiocytosis, generalized lymphomas of low-grade pathology, salvage chemotherapy, immunotherapy, treatment in children, and long-term complications of therapy. (112 Refs)

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
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HE 20. 3173/2:

HODGKIN'S DISEASE: DIAGNOSIS AND STAGING

1. HODGKIN'S DISEASE: A CLINICOPATHOLOGIC STUDY OF 659 CASES.

Colby TV, Hoppe RT, Warnke RA
Dept. Pathology, Stanford Univ. Medical Center, Stanford, CA
Cancer; 49(9):1848-1858 1982

A large number of histologic and clinical parameters were assessed, tabulated and intercorrelated in 659 patients with Hodgkin's disease evaluated and treated at Stanford University Medical Center. Nodular sclerosis was the most common pattern (60%) and also had the best total survival, but lymphocyte predominance had the best relapse-free survival. While a number of histologic parameters showed a significant correlation with relapse-free survival, multivariate analysis showed that age, stage, and treatment were relatively more important. Of the histologic parameters, only the number of lymphocytes, fibroblasts, and amount of sclerosis remained significant after multivariate analysis. The positive correlation of sclerosis, negative correlation of the number of fibroblasts and lack of correlation of lacunar cells with relapse free survival in patients with nodular sclerosis suggested that the type of mesenchymal reaction was of prime importance in determining prognosis in that form of Hodgkin's disease. The number of lymphocytes did not independently affect prognosis in patients with nodular sclerosis but did so for the entire group. The cellular phase of nodular sclerosis was found to have an overall survival and some clinical features more akin to mixed cellularity Hodgkin's disease. (Author abstract) (44 Refs)

2. IS STAGING LAPAROTOMY FOR HODGKIN'S DISEASE STILL JUSTIFIED?

Nelson PW, Townsend CM, Eakin DL, Costanzi JJ
(c/o Townsend) Dept. Surgery, Univ. Texas Medical Branch, Galveston, TX, 77550
Am J Surg; 143(3):288-292 1982

The records of 50 consecutive patients who underwent staging laparotomy for Hodgkin's disease were reviewed. Preoperative clinical stages were as follows. Stage I, 12 patients; Stage II, 20 patients; and Stage III, 18 patients. The accuracy of preoperative lymphangiography, confirmed pathologically, was 80%. Early experience with computed axial tomographic scanning is promising. The stages of 20 patients (40%) were changed by laparotomy, and their treatment was altered as a result. Fourteen patients were upstaged and 6 downstaged. Patients who were upstaged to Stage IIIB or IV received chemotherapy; those downstaged to Stage I or II received radiotherapy only. Sixty-seven percent of patients with preoperative constitutional symptoms (Class B) had positive findings at laparotomy, compared with only 28% of patients without such symptoms (Class A). Patients with mixed cellularity or lymphocyte-depleted histology were more likely to have positive findings at laparotomy. There were four complications and no operative deaths. We conclude that staging laparotomy retains a useful role in the diagnosis and management of Hodgkin's lymphoma. (Author abstract) (14 Refs)

3. POSTCHEMOTHERAPY STAGING LAPAROTOMY IN HODGKIN'S DISEASE.

Barr LC, Glees JP, McElwain TJ, Peckham MJ, Gazet JC
Royal Marsden Hosp., Downs Road, Sutton, Surrey, England
Br J Cancer; 45(2):174-178 1982

Seventeen patients with Hodgkin's disease who had a staging laparotomy (SL) within 2 mo of the completion of initial chemotherapy are presented. Only one patient had a positive laparotomy. Postchemotherapy SL allows any residual active disease to be assessed, but the incidence of positive findings may be small, and such findings are unlikely to alter subsequent management. SL following chemotherapy is therefore not recommended either for patients in clinical remission or for patients with evidence of relapsed disease. (Author abstract) (6 Refs)

4. GA-67 IMAGING IN HODGKIN'S DISEASE.

Huys J, Schelstraete K, Simons M
Dept. Radiotherapy and Nuclear Medicine, Univ. Hosp., De Pintelaan 135, B-9000 Ghent, Belgium
Clin Nucl Med; 7(4):174-179 1982

In order to answer the question if Ga-67 imaging has a practical utility for the management of the patient with Hodgkin's disease, 108 scans performed on 60 patients were reviewed. When used during the initial staging of the disease or during restaging because of recurrences, Ga-67 imaging - at least in our experience - gave many false negative results in the cervical, axillary and inguinal areas, whereas the majority of true positive scans was found at the mediastinal level (including the lower mediastinum), and also in the lung parenchyma and the upper epigastric regions. Because of its lack of sensitivity, Ga-67 imaging cannot replace other staging procedures, but nevertheless is a valuable adjunctive test, as it can identify tumor localization that may have remained undetected by other methods. Fifty-four scans were performed to monitor treatment with radiation therapy or chemotherapeutic agents. Disappearance or decrease of Ga-67 uptake after treatment usually corresponded to a disappearance or regression of the tumor as ascertained by other methods. When the treatment was shown to be ineffective, Ga-67 uptake persisted or even became more prominent. When, during follow-up, a new concentration of Ga-67 appeared at the original location or elsewhere, a relapse was extremely likely. However, one must be aware of false positive images. In our material, no correlation was found between the intensity of the Ga-67 uptake and the histological subtypes of Hodgkin's disease. Neither did we observe any relation to the blood sedimentation rate or serum iron levels. (Author abstract) (14 Refs)

HODGKIN'S DISEASE: CLINICAL IMMUNOLOGY AND IMMUNOTHERAPY

5. INCREASED SENSITIVITY OF T CELLS TO REGULATION BY NORMAL SUPPRESSOR CELLS PERSISTS IN LONG-TERM SURVIVORS WITH HODGKIN'S DISEASE.

Vanhaelen CP, Fisher RI
(c/o Fisher), Building 10, Room 12N226, NCI, Bethesda, MD, 20205
Am J Med; 72(3):385-390 1982

We have studied the function of T cells in the peripheral blood obtained from long term survivors with Hodgkin's disease in order to determine the sensitivity of those T cells to normal suppressor cell immunoregulatory mechanisms. Concanavalin A-activated suppressor cells from normal donors suppressed the proliferation of lymphocytes obtained from 11 patients (56.8 +-3.5%) and from 28 allogeneic normal control subjects (39.8 +-2.7% [p less than 0.001]). When suppressor monocytes from the normal donors were studied, the mean proliferation of lymphocytes from 19 patients was suppressed 76.3 +-4.8% whereas proliferation of lymphocytes from 26 normal donors was suppressed 46.6 +-4.4% (p less than 0.0001). There was no tendency for the increased sensitivity to suppression that was observed in either assay system to return to normal as the patients' disease free interval increased from 1.5 yr to 12 yr. Furthermore, long-term survivors with diffuse histiocytic lymphoma, who had been treated with comparable chemotherapy, had normal sensitivity to the suppressor monocytes (45.1 +-3.8%). In Hodgkin's disease, the persistent increased sensitivity of T cells to two different normal immunoregulatory cells suggests that the response of the T cell to regulatory signals may be an important cause of the depressed cellular immunity observed in Hodgkin's disease and a clue to the etiology of the disease. (Author abstract) (21 Refs)

6. LYMPHOCYTE FUNCTION IN UNTREATED HODGKIN'S DISEASE: AN IMPORTANT PREDICTOR OF PROGNOSIS.

Wedelin C, Bjorkholm M, Holm G, Ogenstad S, Johansson B, Mellstedt H
Dept. Medicine, Div. Hematology, Danderyd's Hosp., S-182 88 Danderyd, Sweden
Br J Cancer; 45(1):70-79 1982

One hundred and twenty seven consecutive and previously untreated patients with Hodgkin's disease (HD) (mean age 47 years) from the Stockholm area admitted to Radiumhemmet, Karolinksa Hospital, were studied. The age-matched control group consisted of 167 healthy adults. Incorporation of [14C]-dT was measured on Day 1 in unstimulated monocyte-depleted lymphocyte cultures, and on Day 3 in cultures activated by PWM, ConA and PPD. T and B cells were enumerated by surface markers. The patients had significantly decreased relative and total T-cell counts, and the lymphocyte DNA synthesis induced by mitogens and PPD was severely impaired, whilst the spontaneous DNA synthesis was significantly greater than in controls. At follow-up (mean 4 years) 40 patients have died. Deceased patients showed greater spontaneous lymphocyte activation and less response to mitogen and antigen stimulation than the survivors. The 5-year survival of patients with severe lymphocyte impairment was 20%, compared to 80% for the remainder. The lymphocyte tests added prognostic information to that from clinical staging. Disregarding the lack of knowledge of the mechanisms underlying the lymphocyte impairment, we suggest that these relatively simple immunological tests should be included in the clinical evaluation of HD patients and would guide the choice of therapy. (Author abstract) (54 Refs)

7. IMMUNOLOGICAL DATA IN THE CLINICAL EVALUATION OF HODGKIN'S DISEASE.

Burchardt K
Klinika Hematologii, ul. Szkolna 8/12, 60-967 Poznan/VR, Poland
Z Gesamte Inn Med; 36(21):840-842 1981

Pattern of immunological alterations was analyzed in 87 adult patients with Hodgkin's disease. Diagnosis was based on clinical diagnosis and confirmed by lymph node biopsy. Clinical data compared with healthy controls are presented. A decrease in total lymphocyte counts and a diminished count of T-lymphocytes were observed in patients with advanced stages of the disease or in those with radio- or chemotherapeutically induced remissions. Lymphocyte transformation and reactions in skin tests were influenced by the stage of the disease. The cells were below the critical number (500/cubic mm) in the peripheral blood, and inhibition of T-cell function occurred. (21 Refs) (In GER)

8. LYMPH NODE T CELLS IN HODGKIN'S DISEASE: ANALYSIS OF SUSPENSIONS WITH MONOCLONAL ANTIBODY AND ROSETTING TECHNIQUES.

Aisenberg AC, Wilkes BM
Huntington Lab., Massachusetts General Hosp., Boston, MA, 02114
Blood; 59(3):522-527 1982

Suspensions prepared from lymph nodes involved by Hodgkin's disease and from a diverse group of lymph node hyperplasias were investigated with a panel of 10 monoclonal antibodies and a variety of conventional surface marker techniques. In both Hodgkin's disease and hyperplasia, 60%-70% of the cells were T lymphocytes, approximately 80% of the inducer/helper subset and 20% of the cytotoxic/suppressor subset. The most prominent differences observed between Hodgkin's disease and hyperplastic T cells are explained by greater affinity of the sheep cell receptor on the surface of the lymphoma T lymphocytes. This greater affinity was best demonstrated by the formation of rosettes with unsensitized or immunoglobulin-sensitized sheep erythrocytes after incubation at 37 C, an occurrence observed only with Hodgkin's disease cells. In addition, in hyperplasia, a variable proportion of lymphocytes reacting with the anti-T-cell monoclonal antiserum OKT3 failed to form unsensitized rosettes at 4 C (E rosettes), while in Hodgkin's disease there was near equivalence of T cells that reacted with the antiserum and formed E rosettes. In addition to the increased infinity for sheep erythrocytes, some Hodgkin's disease specimens displayed increased reactivity with the monoclonal antibody OKM1, which detects monocytes and granulocytes, and the monoclonal antibody OKT10, which reacts with early thymocytes. Finally, 14 of 20 lymphoma samples exhibited polar migration of the fluorescent material (capping) with one or more antisera (most frequently OKI1, the monoclonal antibody with specificity for the Ia-like antigen). These findings are useful in distinguishing Hodgkin's disease lymph nodes from hyperplasia by surface marker characteristics and may be relevant to older observations that Hodgkin's disease T cells aggregate about Reed-Sternberg cells. (Author abstract) (26 Refs)

9. NATURAL KILLER ACTIVITY IN SPLEENS AND LYMPH NODES FROM PATIENTS WITH HODGKIN'S DISEASE.

Ruco LP, Procopio A, Uccini S, Marcorelli E, Baroni CD
IV Cattedra di Anatomia ed Istologia Patologica, Universita di Roma,
Viale Regina Elena 324, 00161 Roma, Italy
Cancer Res; 42(5):2063-2068 1982

Natural killer (NK) activity against K-562 myeloid cell line was evaluated in 21 spleens and 14 lymph nodes from patients with Hodgkin's disease (HD). NK activity of eight HD-involved (HD-) spleens [556 lytic units (LU)] was found five-fold higher than that of 13 HD-uninvolved (HD-) spleens (112 LU) (p less than 0.01). Moreover, NK activity of HD+ spleens was significantly different (p less than 0.05) from that of three spleens involved by non-HD lymphoma (100 LU). NK activity of four spleens from nonneoplastic patients (250 LU) was intermediate between those of HD+ and HD- spleens. Lymph node cells were about 10-fold less cytotoxic. NK activity of seven HD+ lymph nodes (43 LU) was three-fold higher than that of three lymph nodes involved by non-HD lymphoma (8 LU). However, these differences were not statistically significant. Our data are compatible with increased NK activity in HD+ tissues as well as with depressed NK activity in HD- tissues. The observation that NK activity of peripheral blood leukocytes from nine HD patients (116 LU) (p less than 0.05 only at 100:1 effector:target cell ratio) may support the latter interpretation. Partial characterization of effector cells in HD+ and in HD- spleens indicated that, in both instances, NK cells were nonadherent and almost equally distributed between the erythrocyte-negative and -positive cell fractions. Finally, NK activity of both HD+ and HD-spleen cells could be further potentiated in vitro by interferon. (Author abstract) (30 Refs)

10. SUPPRESSIVE EFFECT OF ADHERENT MONONUCLEAR CELLS FROM PERIPHERAL BLOOD OF PATIENTS WITH HODGKIN'S DISEASE ON PHA RESPONSIVENESS.

Moghe MV, Advani SH, Gangal SG
Immunology Div., Cancer Res. Inst., Tata Memorial Centre, Bombay
400 012, India
Indian J Exp Biol; 19(12):1101-1106 1981

The possible suppressive effect of adherent cells from peripheral blood mononuclear cells (PBMNC) of patients with Hodgkin's disease (HD) on phytohemagglutinin (PHA) responsiveness of lymphocytes from healthy donors was investigated using allogeneic co-cultures. PBMNC were obtained from 22 untreated HD patients. Depletion of adherent cells from HD PBMNC resulted in three different responses: decreased PHA response compared with that of normal donors (27%), increased PHA responsiveness (27%) indicating monocyte-induced suppression, and no change in PHA responsiveness (45%) suggesting that suppressor cells could exist in the nonadherent population. Adherent cells from all categories caused depression in mitogen responsiveness of normal lymphocytes. Following depletion of autochthonous adherent cells, the addition of normal adherent cells appeared to augment the mitogen response in 75% of HD patients. These results demonstrate that the mitogen response of HD lymphocytes may be influenced by the balance between subpopulations of monocytes rendering suppression and help in addition to suppressor lymphocytes. In 69% of tests with normal adherent cells, the monocytic help provided to HD lymphocytes was abrogated by the addition of carageenan; with HD adherent cells, such an effect was observed in only 47% of tests. Thus, under the experimental conditions used, normal monocytes were inactivated to a greater extent than HD monocytes by the same dose of carageenan. HD monocytes may have different phagocytic activity and lysosomal differentiation required for activity of carageenan. (26 Refs)

11. SERUM FACTORS INHIBITING SOME LEUKOCYTIC FUNCTIONS IN HODGKIN'S DISEASE.

Petrini M, Azzara A, Polidori R, Vatteroni ML, Caracciolo F, Carulli
G, Ambrogi F
Istituto di Patologia Speciale Medica 3, Univ. Pisa, Pisa, Italy
Clin Immunol Immunopathol; 23(1):124-132 1982

The presence of leukocyte inhibitory factor(s) (S-LIF) in the serum of patients with Hodgkin's disease (HD) has been investigated. It was possible to demonstrate the inhibitory activity in 50% of the patients by employing the agarose plate method. The PHA response in these patients has been found to be reduced. A linear correlation exists between this reduction and the presence of S-LIF in the sera. In order to assess some biological properties of these sera, chemotaxis and phagocytosis of normal cells in the presence of sera from patients with HD have been investigated and both these leukocyte functions have been found to be reduced. The inhibitory capacity was detectable in the same sera which exhibited S-LIF activity and a close linear correlation could be shown. In order to assess whether S-LIF had the same properties of in vitro produced LIF, two monosaccharides were added: L-fucose, capable of blocking the inhibitory activity of LIF, and glucose, which does not block this activity. Surprisingly the addition of L-fucose and glucose greatly enhanced the inhibitory activity of S-LIF. These observations clarify the relationship between the presence of S-LIF and the immunological status in patients with HD and give some indications of the characterization of this (these) factor(s). (Author abstract) (24 Refs)

HODGKIN'S DISEASE: CHEMOTHERAPY

12. ALTERNATING DRUG COMBINATIONS IN THE TREATMENT OF ADVANCED HODGKIN'S DISEASE.

Santoro A, Bonadonna G, Bonfante V, Valagussa P
(c/o Bonadonna) Istituto Nazionale Tumori, Via Venezian, 1-Milan
20133, Italy
N Engl J Med; 306(13):770-775 1982

From 1974-1980, 75 consecutive patients (16-63 yr old) with initial Stage IV Hodgkin's disease (55 patients) or extranodal relapse (20 patients) after primary radiotherapy were randomly allocated to receive either 12 monthly cycles of mechlorethamine, vincristine, procarbazine, and prednisone (MOPP: 38 patients), or six cycles of MOPP alternating monthly with six cycles of doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD: 37 patients). In patients with complete response (CR) after 12 cycles of therapy, no additional treatment was administered. In those with partial response, treatment was continued at the maximal tolerated doses until either complete remission or progressive disease occurred. Remission rates in the two treatment groups were compared. CR was achieved in 71% of the patients treated with MOPP and in 92% of those given MOPP alternating with ABVD. Comparative analysis of results indicates that the alternating treatment was superior to MOPP alone in all subgroups, except for those with disease in multiple extranodal sites. The median relapse-free survival in the MOPP group (27 patients with CR) was 20 mo, whereas that in the MOPP-plus-ABVD group (34 CR) was in excess of 31 mo. The analysis of total survival indicated that 5 yr from the beginning of chemotherapy, 61% of patients in the MOPP group and 83% in the MOPP-plus-ABVD group remained alive. Toxic effects in each treatment group were compared. Vomiting and hair loss were more frequent and severe after chemotherapy with MOPP plus ABVD. With regard to marrow tolerance, MOPP plus ABVD was better tolerated than MOPP alone. (19 Refs)

HODGKIN'S DISEASE: MULTIMODAL THERAPY

13. ABSENCE OF TREATMENT-INDUCED SECOND NEOPLASMS AFTER ABVD IN HODGKIN'S DISEASE.

Valagussa P, Santoro A, Bellani FF, Franchi F, Banfi A, Bonadonna G
(c/o Bonadonna), Istituto Nazionale Tumori, Via Venezian 1, 20133 Milano, Italy
Blood; 59(3):488-494 1982

One of the most serious complications of successful treatments for Hodgkin's disease is an increased incidence of acute nonlymphocytic leukemia (ANLL) and other malignancies. A retrospective analysis carried out on 1,032 consecutive patients with Hodgkin's disease admitted to our Institute between 1965 and 1978 and treated with radiotherapy (RT) or chemotherapy or both modalities revealed that within 19 yr from initial therapy, ANLL was documented in 3% of patients, and over a comparable period of time 7.9% of patients developed other malignancies. ANLL was observed only in patients treated with chemotherapeutic regimens containing alkylating agents and/or procarbazine either alone (2.3%) or associated with RT (4%). Other second tumors were documented in patients given RT with or without chemotherapy. No second malignancies were observed in patients given ABVD (adriamycin, bleomycin, vinblastine, and dacarbazine) with or without RT. The incidence of ANLL was higher in patients given chemotherapy as salvage treatment upon relapse following primary irradiation (6.1%) compared to patients initially treated with combined modality (1.5%). The difference, however, failed to reach statistical significance. Since our analysis supports the evidence of a major role played by alkylating agents, procarbazine, and RT in inducing second malignancies, regimens not containing these drugs or their administration through treatments of different intensity warrant careful consideration. (Author abstract) (39 Refs)

14. THE MANAGEMENT OF STAGE I-II HODGKIN'S DISEASE WITH IRRADIATION ALONE OR COMBINED MODALITY THERAPY: THE STANFORD EXPERIENCE.

Hoppe RT, Coleman CN, Cox RS, Rosenberg SA, Kaplan HS
Dept. Radiology, Div. Radiation Therapy, Stanford Univ. Medical Center, Stanford, CA, 94305
Blood; 59(3):455-465 1982

At Stanford University, between 1968 and 1978, 230 patients with pathologic Stage I-II Hodgkin's disease were treated on prospective clinical trials with either irradiation alone or irradiation followed by six cycles of adjuvant combination chemotherapy. The actuarial survival at 10 yr was 84% for patients in either treatment group. Freedom from relapse at 10 yr was 77% among patients treated with irradiation alone and 84% after treatment with combined modality therapy [p(Gehan) = 0.09]. Freedom from second relapse at 10 yr was 89% and 94%, respectively [p(Gehan) = 0.56]. Several prognostic factors were evaluated in order to identify patients at high risk for relapse or with poor ultimate survival after initial treatment with irradiation alone. Systemic symptoms, histologic subtype, age, and limited extranodal involvement (E-lesions) did not affect the prognosis of patients and failed to identify patients whose survival could be improved by the routine use of combined modality therapy. Patients with large mediastinal masses (mediastinal mass ratio greater than or equal to 1/3) had a significantly poorer freedom from relapse when treated with irradiation alone than when treated initially with combined modality therapy [45% versus 81% at 10 yr, p(Gehan)=0.03]. The 10-yr survival of these patients, however, was not significantly different (84% versus 74%). The implications of these observations on the management of patients with early stage Hodgkin's disease are discussed. (Author abstract) (34 Refs)

15. HODGKIN'S DISEASE: TREATMENT WITH LOW DOSE RADIATION AND CHEMOTHERAPY.

Donaldson SS
Dept. Radiology, Div. Radiation Therapy, Stanford Univ. Sch. Medicine, Stanford, CA, 94305
Front Radiat Ther Oncol; 16:122-133 1982

After staging laparotomy and splenectomy, 48 children with Hodgkin's disease were given low-dose radiotherapy (RT: 1,500-2,500 rads according to bone age) and six cycles of MOPP therapy (nitrogen mustard, vincristine, procarbazine, and prednisone). Prednisone was omitted if mantle RT was given. Involved-field RT was given to Stage IA and IIA patients, total lymphoid RT (TLR) to Stage IB-IIIsA patients, and maintenance MOPP to Stage IV patients with bone marrow involvement (IVm). Booster RT (3,000-3,500 rads) was given to 159 nodal sites (not overlying the axial skeleton) which did not regress completely after RT and/or MOPP therapy. One of these nodal sites recurred after 18 mo and regressed after further RT; the patient remained recurrence-free (NER) thereafter. Two Stage IVm patients failed to respond to treatment and died within 6 mo. The other 46 patients were alive and 45/46 were continuously NER after a median of 3 yr. A few patients remained NER and showed no detectable developmental abnormalities after 10 yr of follow-up. The early side effects of treatment, including thyroid dysfunction in 4/24 children tested, were reversible and not severe. Shielding was applied to prevent RT damage to the heart, lungs, and gonads, apparently with success. The late effects of RT on bone growth were directly proportional to the dose and vol and inversely proportional to the patient's age at diagnosis. High-dose TLR led to a disproportionate change in sitting height as compared to standing height, especially in patients treated in early childhood (less than 6 yr old) or adolescence. The number of prepubertal boys was too small and the follow-up time too short to assess the effects of MOPP on testicular function. No second malignancies were noted during the follow-up period. (27 Refs)

16. EFFECTS OF MANTLE-FIELD IRRADIATION AND CHEMOTHERAPY ON RESPIRATORY FUNCTION.

Dixsaut G, Teillet F, Dana M, Miot C, Catherine N, Teillet-Thiebaud F
Service d'Explorations Fonctionelles, Hopital Louis Mourier, F 92701 Colombes Cedex, France
Nouv Presse Med; 11(6):429-432 1982

In 15 patients with mediastinal Hodgkin's disease treated with chemotherapy followed by mantle-field irradiation respiratory function tests performed before and after irradiation showed a decrease in vital capacity and FEV1 as compared with pretreatment values. The decrease was maximum at 4 mo and regressed over 1 yr. No significant changes were observed in blood gas measurements. Respiratory symptoms, which were frequent after irradiation, almost completely disappeared within 1 yr. The therapeutic combination had no cumulative adverse effect on respiratory function. (Author abstract) (20 Refs) (In FRE)

MALIGNANT LYMPHOMA: DIAGNOSIS AND STAGING

17. SCLEROSIS IN DIFFUSE HISTIOCYTIC LYMPHOMA: A CLINICOPATHOLOGIC STUDY OF 25 CASES.

Ree HJ, Leone LA, Crowley JP
Dept. Pathology, Rhode Island Hosp., Providence, RI, 02902
Cancer; 49(8):1636-1648 1982

Sclerosis was observed in the lymph node specimens of 26 of 57 (46%) patients with diffuse histiocytic lymphoma. Two major types of sclerosis were observed: 'compartmentalizing' (56%), in which the tumor was divided into many small compartments by anastomosing, hyalinized stroma; and 'diffuse' (44%), in which the sclerosis occurred without evident partitioning of the tumor. The hyalinized stroma of the compartmentalizing sclerosis was frequently continuous with small vessels accompanied by aggregates of small lymphocytes, suggesting that the sclerosis was related to the occurrence of small lymphocyte-associated postcapillary venules. Compartmentalizing sclerosis was further divided into two groups: The first group (even pattern) was characterized by an orderly occurrence of the stromal network with no evidence of distortion, evenly spaced tumor cells showing no axis in their arrangement, and a sharp demarcation of tumor cells from the stroma. The second group (uneven pattern) was marked by either a disorderly occurrence of the stromal network with distortion of the overall pattern, tumor cells arranged along an axis, or poor demarcation of tumor cells from the stroma with individual envelopment of tumor cells by the stroma. Approx two-thirds of the patients (9/14) with the compartmentalizing sclerosis survived 2 yr or more after diagnosis; most patients (10/11) with diffuse sclerosis died within 2 yr. Compartmentalizing sclerosis, even pattern, was associated with a consistently favorable prognosis; the uneven pattern was not. This study indicates a marked variation in the survival of patients with diffuse histiocytic lymphoma with sclerosis and demonstrates that prognostic subgroups may be delineated by additional morphologic features. (Author abstract) (16 Refs)

18. SCLEROSIS IN FOLLICULAR LYMPHOMAS.

Bak M, Szentirmay Z, Toth J
Onkopathologiai Kutato Intezet, Orszagos Onkologiai Intezet, Rath Gy, u. 7-9, 1123 Budapest, Hungary
Morphol Igazsagugyi Orv Sz; 22(1):60-63 1982

Sclerosis was found in 41 patients (22 men and 19 women) in a group of 151 patients with follicular non-Hodgkin's lymphomas originating in lymph nodes. The incidence of sclerosis was 20/96 for patients with follicular lymphomas, 16/41 for those with follicular-diffuse lymphomas, and 5/14 for those with diffuse lymphomas. Twenty-six of the 41 patients with sclerosis were in the age bracket 50-69 yr. Two types of sclerosis were distinguished: in Type I, the affected lymph node was divided into irregular nodules of varying sizes by hyalinized, birefringent collagen bundles with thicknesses of 10-100 microns; in many cases, the connective-tissue bundles penetrated the pericapsular fatty tissue; this type of sclerosis was encountered in both follicular and diffuse centroblastic-centrocytic lymphomas, and Type II (narrower collagen connective tissue of reticular pattern, fine collagen bundles forming septa and surrounding smaller clusters of tumor cells in some cases) was seen mainly in diffuse lymphomas. Joint occurrence of both types of sclerosis was seen in four patients. The overall 5-yr survival rate of the 151 patients was 49%; 41% for the patients without sclerotic lymph nodes and 68% for those with sclerosis, ie, it was considerably higher for the latter. Sclerosis occurring in malignant lymphomas is considered to be a peculiar reaction of the host, inhibiting tumor spread. (13 Refs) (In HUN)

19. RADIOLOGIC FEATURES OF INTRATHORACIC LYMPHOMA.

Stark P
Dept. Radiology, Massachusetts General Hosp., Boston, MA
Appl Radiol; 11(2):75-77,80,82-83,85-87 1982

Radiologic features of intrathoracic lymphoma are discussed. The most common intrathoracic presentation of Hodgkin's disease is lymphadenopathy in the mediastinum, hilar regions, or both, initially found in almost half of patients. The lung parenchyma may eventually be involved in up to 40% of cases; spreading occurs along the efferent lymphatics which parallel the bronchovascular bundles. In non-Hodgkin's lymphoma, the thorax is the primary site in only 4% of cases, but lung involvement is eventually seen in up to 50%. The superior and anterior compartments are involved in about 45% of cases of non-Hodgkin's lymphoma, compared to 90% of Hodgkin's disease cases. Nonmalignant lymphoid disorders pose problems in differential diagnosis, including lymphocytic interstitial pneumonitis, pseudolymphoma, lymphomatoid granulomatosis, giant follicular hyperplasia, and immunoblastic lymphadenopathy. In differential diagnosis of lung parenchymal lymphoma, the following entities should be considered: infection, pulmonary infarction, drug reaction, pseudolymphoma, bronchioalveolar carcinoma, alveolar sarcoidosis, and lipid pneumonia. Routine x-ray examination supplemented by chest fluoroscopy, including a barium swallow, will outline most cases of intrathoracic lymphoma. Gallium 67 scanning, full lung tomography, and computed tomography are useful in diagnosis. (12 Refs)

20. ROENTGENOGRAPHIC ASPECTS OF NON-HODGKIN'S LYMPHOMAS PRESENTING WITH OSSEOUS LESIONS.

Spagnoli I, Gattoni F, Viganotti G
Dept. Radiology, Natl. Cancer Inst., Milan, Italy
Skeletal Radiol; 8(1):39-41 1982

Cases of all patients with non-Hodgkin's lymphoma (NHL) treated at the National Cancer Institute of Milan, Italy, during the period 1968-1977, were assessed for incidence of bone involvement. Radiographs taken from a total of 992 previously untreated patients indicated bone involvement in 61 cases. Of the 61 patients, 10 showed only single bone involvement and were classified as primary NHL of bone. The remaining 51 patients showed involvement of more than one bone or of one affected bone plus lymph node and/or visceral lymphomatous lesions. Results indicated that primary lymphoma of bone prefers the appendicular skeleton, especially the femurs, while the axial skeleton is more affected when the disease has spread. Osteolysis was the principal radiological sign, being present in more than two thirds of the cases examined. This lesion type unfortunately gives no specific sign of its lymphomatous nature. Roentgenographic evidence indicate that cortical destruction or soft tissue involvement has an adverse prognostic value. Although bone involvement in previously untreated NHL is an uncommon presenting sign, these results indicate that such involvement is sufficiently frequent to justify routine skeletal x-ray survey during initial staging. (12 Refs)

21. MALIGNANT LYMPHOMA SIMULATING LYMPH NODE TOXOPLASMOSIS.

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Dept. Pathology, Univ. Helsinki, Haartmaninkatu 3, SF-00290 Helsinki 29, Finland
Histopathology; 6(2):129-140 1982

The difficulties in differential diagnosis between lymph node toxoplasmosis and malignant lymphoma are discussed; histological examination of 667 cases with original diagnoses of toxoplasmosis (TOX) or the suspicion of TOX was performed with no knowledge of clinical, serological, or follow-up data. Four hundred and three cases were reclassified as probable TOX, 236 as some other benign disorder, 12 as malignant lymphoma, and 15 as atypical hyperplasia (AH). Eight cases were considered Hodgkin's disease, lymphocytic predominance, nodular subtype (HDLPN); two were HD, lymphocytic predominance, diffuse subtype; and two were HD, nodular sclerosing type. Usually, TOX is accompanied by preservation of follicular structure but marked hyperplasia at germinal centers, while malignant lymphoma exhibits destruction of the lymph node structure and germinal centers are not visible. When diagnostic difficulties arise, a diagnosis of TOX is favored by a general appearance of reactive hyperplasia, the presence of epithelioid cell clusters inside the germinal centers, and the presence of strands of monocytoid cells. In HDLPN, the nodules are usually rounded and evenly distributed, while in TOX the nodules represent hyperplastic germinal centers and are often irregularly shaped and unevenly distributed. In TOX, the nodules demonstrate the characteristic cytology of hyperplastic germinal centers, while in HDLPN they are composed of epithelioid cells and normal-appearing small lymphocytes, L and H type Reed-Sternberg cells, and, occasionally, classical Reed-Sternberg cells. AH was the most common condition misdiagnosed as TOX; one-half of AH cases later developed a malignant lymphoma. (14 Refs)

22. NON-HODGKIN'S MALIGNANT LYMPHOMAS: A CYTOLOGIC CLASSIFICATION BASED ON STATISTICAL ANALYSIS AND CORRELATED WITH PROGNOSIS.

Sotto JJ, Caillot P, Sotto MF, Brambilla E, Lachet B, Michallet M, Martin H, Bensa JC, Schaerer R, Seigneurin D, Hollard D
Groupe Hospitalier des Affections Sanguines et Tumorales, CHRU de Grenoble, B.P. 217 X, F-38043 Grenoble Cedex, France
Anal Quant Cytol; 4(1):6-24 1982

Based on cytological study of 144 patients with non-Hodgkin's malignant lymphoma (NHML), a cytologic classification with 52 categories was established on the basis of certain physical variables, staining reactions and mitotic activity. Variables include diameter of cells, nuclear-cytoplasmic ratio, shape of nucleus, appearance of chromatin, features pertaining to the nucleoli, cytoplasmic outline and other features of cytoplasm, naked nuclei, cytoclasis, mitosis, and normal lymphocytes. A stepwise discriminant analysis was performed on the cytologic classification system to determine the best variables for separating the classes. The use of these characteristics renders the classification reproducible and applicable to clinical practice. The categories comprise three groups (1, 2 and 3) containing nine classes (1A, 1B, 1C; 2A, 2B, 2C; 3A, 3B, 3C). A comparison was made between cytologic classes and the NHML patients grouped according to their clinical courses. Of the patients in classes 2A, 2B and 2C, 94% showed characteristics of acute leukemia. Poor prognosis or metastatic patterns were shown by 78% of patients in classes 3A, 3B and 3C. A pattern indicative of good prognosis was shown by 76% of those in classes 1A, 1B and 1C. (41 Refs)

23. A COMPARATIVE STUDY OF BURKITT'S AND NON-BURKITT'S 'UNDIFFERENTIATED' MALIGNANT LYMPHOMA: IMMUNOLOGIC, CYTOCHEMICAL, ULTRASTRUCTURAL, CYTOLOGIC, HISTOPATHOLOGIC, CLINICAL AND CELL CULTURE FEATURES.

Grogan TM, Warnke RA, Kaplan HS
Dept. Pathology, Univ. Arizona, Coll. Medicine, Tucson, AZ, 85724
Cancer; 49(9):1817-1828 1982

Nine patients with 'undifferentiated' lymphoma (DUL) of Burkitt's (AMB, 4 cases) and non-Burkitt's (NB, 5 cases) types were studied. All specimens stained for a single immunoglobulin light chain indicating a monoclonal B-cell lymphoid proliferation. Striking methyl green pyronine and punctate Oil-Red-O staining were demonstrated in both groups. Histologic and cytologic examination demonstrated a lymphoid proliferation with a high mitotic count, a 'starry-sky' pattern, prominent cytoplasmic basophilia and vacuolation in both subtypes. The AMB cases showed a predominance of regular nuclei with 3-5 basophilic nucleoli, while the NB cases showed slightly greater nuclear variability with a greater proportion of nuclei containing 1-2 eosinophilic nucleoli. The AMB patients were all children (median, age 12 yr) and those with NB were adults (median, age 54 yr). The site of presentation in both groups was predominantly extranodal and abdominal. This report emphasizes the considerable immunologic, morphologic, cytochemical and clinical overlap present among the subtypes of 'undifferentiated' lymphoma. (Author abstract) (41 Refs)

24. HEPATIC HUMORAL AND MORPHOLOGIC STUDY IN NON-HODGKIN'S LYMPHOMA.

Garay GE, Zeilikoff R, Richard LA, Baljetti N, Koch O, Domecq P, Brush E, Pavlovsky S
Departamento de Oncohematologia, Academia Nacional de Medicina, Buenos Aires, Argentina
Medicina (B Aires); 41(Suppl):49-56 1981

Hepatic (HE) humoral and morphologic study was performed in 21 untreated patients (14 males, 7 women; 28-71 yr old) with non-Hodgkin's lymphoma; 12 had good and 9 had bad histologic prognosis according to Rapapport's classification. According to Ann Arbor clinical staging, 2 patients were Stage Ia, 3 were Stage IIa, 3 were Stage IIb, 8 were Stage IIIa, 2 were Stage IIIb, 3 were Stage IVa, and 2 were Stage IVb. Tests performed included percutaneous HE biopsy, echography, bromosulfophthalein clearance, protein and prothrombin time, HE enzymes, surface antigen, surface antiantigen antibody (AA) and hepatitis B core AA and autoantibodies. HE biopsy failed in 4/17 patients, 5/17 were normal, 3/17 showed HE lymphomatous infiltrations (HLI), 7/17 fatty changes, 1/17 mild cholestasis, and 1/17 vacuolization and nuclear anisokaryosis. Echography indicated changes in patients with HLI. Prothrombin time and K1 were most indicative parameters for HLI and other non specific morphologic changes. Phosphohexose isomerase and lactic acid dehydrogenase were increased in lymphomatous disease, but not in HE disease; they decreased in patients, who were in complete remission (CR) after receiving polychemotherapy Patients, who did not achieve CR or died (almost half), showed significant number of changes in HE function in contrast to those in CR. (31 Refs) (In SPA)

25. URINARY EXCRETION OF MONOACETYL POLYAMINES IN PATIENTS WITH NON-HODGKIN'S LYMPHOMA.

Abdel-Monem MM, Merdink JL, Theologides A
Dept. Medicinal Chemistry, Coll. Pharmacy, Univ. Minnesota, Minneapolis, MN, 55455
Cancer Res; 42(5):2097-2098 1982

The pretreatment concentrations of polyamines were determined in the 24-hr urine of 14 patients with widespread non-Hodgkin's lymphoma. In 10 of 14 patients, the ratio of N1-acetylspermidine to N8-acetylspermidine was significantly higher than the mean for normal subjects. These results confirm our previous observations that the urinary excretion of N1-acetylspermidine is increased in some patients with lymphoma and suggest that the determination of urinary acetyl polyamines may be useful in conjunction with other procedures in the diagnosis of lymphoma. The ratio of N1-acetylspermidine to N8-acetylspermidine in the postchemotherapy 24-hr urine was 25 in one patient who had diffuse histiocytic lymphoma. This is the highest ratio ever reported. The patient responded well to chemotherapy, and rapid lysis of lymphoma lesion was observed. The potential utility of the rapid increase in the ratio of N1-acetylspermidine to N8-acetylspermidine as a criterion of tumor lysis is of interest and is currently under further investigation. (Author abstract) (10 Refs)

MALIGNANT LYMPHOMA: CLINICAL IMMUNOLOGY AND IMMUNOTHERAPY

26. IMMUNOLOGICAL CHARACTERIZATION OF NON-HODGKIN'S LYMPHOMA: ENRICHMENT OF NEOPLASTIC CELLS FROM LYMPHOID TISSUES AND BLOOD.

Bom-Van Noorloos AA, Van Beek AA, Ubels-Postma J, Zeijlemaker WP, Van Heerde P, Von Dem Borne AE, Cleton FJ, Melief CJ
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Cancer; 49(8):1605-1612 1982

Cell suspensions prepared from lymph nodes, spleen or peripheral blood of patients with non-Hodgkin's lymphoma (NHL) often contain a high percentage of residual nonmalignant cellular elements. By E-rosette sedimentation, it was possible to enrich such suspensions from patients with various types of lymphoma for malignant cells. In patients with a B- or non-B/non-T-cell lymphoma, the neoplastic cells were found in the non-T fraction. The capacity to respond to stimulation by various stimuli was then confined to the T-cell fraction, which contained the residual normal T-cells. In patients with T-cell lymphomas, in which the malignant cells had retained the capacity to form E-rosettes, lymphoma cells were found in the T fraction. These cells usually did not respond to mitogenic stimuli. Using this separation method, small proportions of neoplastic cells could be identified in mixed cell populations. Thus, in the blood from 9 out of 23 lymphoma patients without abnormalities in routine blood tests, a population of abnormal cells was detected after cell separation. This included a monoclonal B-cell population in the blood of four patients, a questionably monoclonal B-cell population in the blood of two patients and an increased non-B/non-T cell population in the blood of three patients. (Author abstract) (35 Refs)

27. IMMUNOLOGIC CHARACTERIZATION OF A HELPER T-CELL LYMPHOMA.

Gramatzki M, Dolan MF, Fauci AS, Maples JA, Bonnard GD, Strong DM
(c/o Strong) Tissue Bank, Naval Medical Res. Inst., Bethesda, MD, 20814
Blood; 59(4):702-708 1982

The lymphocytes of a patient with a T-cell non-Hodgkin's lymphoma with peripheral blood involvement and polyclonal hypergammaglobulinemia were characterized in terms of surface markers and immunologic functions. Using the fluorescence-activated cell sorter and employing various monoclonal antibodies against T-cell surface antigens, it was shown that almost all of the patient's peripheral blood lymphocytes were positive for OKT4 and 9.3, antibodies that recognize helper T-cell subset. The circulating lymphoma cells had typical characteristics for T cells; they formed spontaneous rosettes with sheep erythrocytes and stained with the pan T-cell antibodies 9.6 and 10.2, but did not react with other anti-T-cell monoclonal reagents such as OKT3, UCHT-1, and 3A1. The cells appeared to be mature by the fact that they did not stain with OKT6, and terminal deoxynucleotidyl transferase was undetectable. Functionally, they were able to provide 'help' for antibody production, and they could be stimulated to produce moderate amounts of interleukin-2, while unable to proliferate in response to mitogens. Morphologically, some of the lymphocytes showed a deeply cleaved nucleus. (Author abstract) (53 Refs)

28. CHANGES IN SURFACE ANTIGENS ON MALIGNANT T CELLS FROM LYMPHOBLASTIC LYMPHOMAS AT RELAPSE: AN APPRAISAL WITH MONOCLONAL ANTIBODIES AND MICROFLUOROMETRY.

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Blood; 59(4):809-815 1982

By using a panel of monoclonal antibodies reactive with lymphoid differentiation antigens and microfluorometry, we investigated the malignant cells from five patients with T-cell lymphoblastic lymphoma both at initial involvement and at relapse. We have observed changes in cell surface antigens densities in four of the five cases. These changes could be interpreted as a shift in the status of differentiation of the malignant cells. In two cases the malignant cells appeared to be arrested at an earlier stage at relapse than at initial involvement, while in the two other cases, cells at relapse appeared to be arrested at a later stage than at initial involvement. Interestingly, a parallelism was observed between regression of the differentiative status of the malignant T cells and 'leukemic conversion.' These observations are also relevant to the understanding of the development of tumor resistance to chemotherapy. (Author abstract) (39 Refs)

29. A MONOCLONAL ANTIBODY DEFINING A BURKITT LYMPHOMA ASSOCIATED ANTIGEN.

Wiels J, Fellous M, Lenoir G, Tursz T

Laboratoire de Immunologie, Clinique Institut G. Roussy, 94800 Villejuif, France

Protides Biol Fluid Proc Colloq; 29:899-902 1982

Reactivity of monoclonal antibody 38-13, obtained by fusing murine myeloma cells with Lewis rat splenocytes sensitized with Daudi cells (human Burkitt lymphoma), was investigated. Negative results were obtained in all patients with B chronic lymphoid leukemia, acute lymphoid leukemia (T and nonT-nonB), acute myeloid leukemia, acute monoblastic leukemia, Hodgkin's disease, T cell lymphosarcoma, and B cell lymphosarcoma (nodular and diffuse). Positive results were observed in 4/8 patients with B cell Burkitt lymphoma. When the specific reactivity of 38.13 ascites was tested with a panel of cell lines of various origins, both by complement dependent lymphocytotoxicity tests and indirect membrane immunofluorescence assays, all the positive target cells were of Burkitt's lymphoma origin. Negative results were obtained with 15 Epstein-Barr virus positive lymphoblastoid cell lines, 4 T cell lines, a chronic myelogenous leukemia cell line, 4 teratoma cell lines, and one each of melanoma and neuroblastoma. The 38.13 monoclonal antibody may be useful for diagnosis and specific immunotherapy of Burkitt lymphomas. (8 Refs)

30. MONOCLONAL ANTIBODY AGAINST A MEMBRANE ANTIGEN CHARACTERIZING LEUKEMIC HUMAN B-LYMPHOCYTES.

Forster HK, Gudat FG, Girard MF, Albrecht R, Schmidt J, Ludwig C, Obrecht JP

Pharma Res. Div., F. Hoffmann-La Roche and Co., Ltd., Basel, Switzerland

Cancer Res; 42(5):1927-1934 1982

In the diagnosis of non-Hodgkin's lymphomas, the ready characterization of the neoplastic cell lineage by analysis of cell surface markers is of great importance. We present evidence for the existence of a human B-leukemia-associated antigen recognized by a complement-fixing monoclonal antibody (anti-Y 29/55). A hybridoma was produced by fusing mouse myeloma cells and splenocytes of a mouse immunized against lymphoid cells of a patient with B-cell chronic lymphocytic leukemia. Characterization of anti-Y 29/55-reactive normal and malignant leukocytes was demonstrated by cytolysis and indirect immunofluorescence. This revealed reactivity with an antigen on B-lymphoma cells (11 patients), on leukemic lymphocytes in B-cell chronic lymphocytic leukemia (13 patients), and on malignant cells in hairy-cell leukemia (2 patients) but not on leukemic cells of T-cell acute lymphoblastic leukemia (1 patient), on T-lymphoma cells (1 patient), on cells of acute myeloblastic leukemia (4 patients), or of chronic myeloid leukemia (4 patients). No specific cytolysis occurred with B- and T-peripheral blood lymphocytes from (a) healthy donors (16 individuals), (b) patient with reactive lymphocytosis (1 patient), (c) nonleukemic multiple myeloma (6 patients), or (d) Hodgkin's disease (3 patients). Surface immunoglobulin-positive, sheep RBC-negative lymphocytes isolated from human spleen (3 individuals), tonsils (7 individuals), and lymph nodes (1 individual), however, we recognized. It is concluded that leukemic B-cells carry a marker characteristic of nonrecirculating sessile B-lymphocytes. (Author abstract) (54 Refs)

31. NON-T, NON-B LYMPHOMAS ARE RARE IN CHILDHOOD AND ASSOCIATED WITH CUTANEOUS TUMOR.

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Blood; 59(3):549-554 1982

Tumor cells from a total of 116 children with non-Hodgkin's lymphoma were studied for their pattern of reactivity with a battery of cell markers, including their capacity for spontaneous formation of sheep erythrocyte rosettes (E-rosettes), demonstration of surface immunoglobulins (SIg), and positivity with antisera against T-cell antigens, the common acute-lymphoblastic-leukemia-associated antigen (cALLa), and Ia-like antigens. Fifty-eight children (50%) had T-cell lymphomas, including all those with mediastinal tumors. Fifty children (43%) had B-cell lymphomas, including 44 of the 45 with abdominal primaries. Eight children (7%) non-T, non-B tumors, four of whom presented at a young age with cutaneous lymphoblastic tumors. These results demonstrate that the great majority of children with NHL, not leukemic at diagnosis, have tumors clearly committed to either T- or B-cell differentiation pathways and only rarely exhibit the common ALL phenotype (cALLa+, Ia+, E-, T-, SIg-), contrasting with the distribution of childhood lymphoblastic leukemias. The unusual association of these non-T, non-B cases with skin involvement has not previously been reported, raising speculation regarding patterns of lymphocyte traffic and origins of childhood lymphomas and leukemias. (Author abstract) (32 Refs)

32. REDUCED NATURAL KILLER CELL ACTIVITY IN NON-HODGKIN'S LYMPHOMA.

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Boll Ist Sieroter Milan; 60(5):394-407 1981

A literature review is followed by a study of the natural killer (NK) activity in 20 patients with non-Hodgkin's lymphoma (NHL) and in 20 age-matched healthy subjects. The NHL patients included 3 with nodular, and 17 with diffuse histology, aged 24-69 yr. All but three were under treatment with multiple chemotherapeutic agents; however, at time of study none had received therapy during the previous 4 wk. Effector cells were lymphocytes separated from cubital vein blood; cells of the K 562 myeloid cell line were used as target cells. Experiments were carried out at effector/target ratios of 20:1 or 40:1 in the 4-hr Cr release assay. Compared with controls, the NHL patients showed reduced NK activity. However, a statistically significant reduction was found only in the group of patients with active disease, either at onset or at relapse. Patients in clinical remission displayed a more moderate decrease of NK cell activity. It is suggested that the study of NK function might be a helpful tool in following the clinical course and efficacy of treatment in NHL. (126 Refs)

33. FIBROBLAST INTERFERON THERAPY IN PATIENTS WITH NON-HODGKIN'S LYMPHOMA (NHL) OF LOW-GRADE MALIGNANCY: PRELIMINARY RESULTS.

Fink U, Siegert W, Huhn D, Wilmanns W, Berdel WE, Emmerich B, Hutsteiner H, Wust I, Rastetter J, Theml H, Riethmuller G
Abteilung Hamatologie und Onkologie, I. Medizinische Klinik, Technische Universitat Munchen, Ismaninger Strasse 22, D-8000 Munchen 80, W. Germany
Blut; 44(2):121-124 1982

Preliminary results of human fibroblast interferon-beta (INF) therapy conducted between 1980-1981 in 10 patients with low-grade malignancy NHL are presented. NHL Grade IV was diagnosed in all patients. All patients received chemotherapy and/or radiotherapy pretreatment at least 4 wk prior to INF therapy. Induction and intensification protocol was followed in nine patients. After completion of intensification, NHL progression was observed in six patients. Treatment was discontinued in five patients. INF therapy was completed in only two patients. A stable disease was observed in a female patient with centroblastic-centrocytic lymphoma (CBCC) after therapy completion. An objective response to therapy was observed in a 45-yr-old male patient with CBCC. The patient was pretreated with nine cycles of cyclophosphamide, vincristine, and prednisolone and 100 rad total body irradiation because of diagnosed peripheral lymphoma, splenomegaly, and bone marrow infiltration. After INF treatment, retrogression of splenomegaly was diagnosed by computed tomography. A minimal residual infiltration (less than 0.1%) and simultaneously myelopoiesis were diagnosed. The therapy effect was classified as a slight partial remission. Most common IFN therapy side effects were fatigue, headache, shivers, and sensation of cold. Granulocytopenia was observed in four patients. (7 Refs) (In GER)

MALIGNANT LYMPHOMA: CHEMOTHERAPY

34. TREATMENT OF ADVANCED DIFFUSE HISTIOCYTIC LYMPHOMA: AN ANALYSIS OF PROGNOSTIC VARIABLES.

Koziner B, Little C, Passe S, Thaler HT, Sklaroff R, Straus DJ, Lee BJ, Clarkson BD
Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Cancer; 49(8):1571-1579 1982

Sixty-five patients with Stages III and IV diffuse histiocytic lymphoma (DHL) were treated with two different and successive combination chemotherapy protocols. Twenty-seven patients were treated with the cyclophosphamide (CTX) L2 protocol, which included maintenance chemotherapy for 3 yr. Thirty-eight patients received the NHL-3 program. Both protocols included radiotherapy (1,350-4,000 rad) to areas of initial bulky disease or persistent tumor, as well as central nervous system prophylaxis with intrathecal methotrexate or cytosine arabinoside in patients with bone marrow involvement. Two-yr survival rates were 44 and 56%, respectively, for the CTX-L2 and NHL-3 protocols. Of the 65 patients, 59 were evaluable for response to therapy. The CTX-L2 produced a 58% total response (TR) rate, 39% complete (CR), and 19% partial (PR). The patients on NHL-3 achieved a TR rate of 82%, 33% CR, and 48% PR. The difference in TR was significant ($p = 0.05$), but in CR was not. Prior chemotherapy ($p = 0.077$) and serum lactic dehydrogenase (LDH) level above 500 U/liter ($p = 0.01$) significantly lessened the chances for achievement of a CR. However, sex, age, the presence of systemic symptoms, stage (III vs IV), and prior RT were not found to be significantly related to CR rate. This analysis suggests that a high level of serum LDH characterizes a subgroup of patients with particularly aggressive DHL that requires a more intensive modality of treatment. (Author abstract) (26 Refs)

35. SALVAGE CHEMOTHERAPY IN RESISTANT MALIGNANT LYMPHOMAS.

Tursz T, Ben Ayed F, Droz JP, Spielmann M, Amiel JL
Service de Medecine A, Institut Gustave-Roussy, rue Camille-Desmoulins, F-94805 Villejuif Cedex, France
Bull Cancer (Paris); 69(1):28-32 1982

A salvage chemotherapy was used in advanced malignant lymphomas resistant to previous chemotherapy. The chemotherapy schedule consisted of the monthly administration of vindesine and continuous infusions of bleomycine, associated with cis-diammine-dichloro-platinum in Hodgkin's disease (patients resistant to MOPP and ABVD protocols) and with DTIC in non-Hodgkin lymphomas (patients resistant to CHOP or equivalent protocol). In 10 patients with advanced Hodgkin's disease (Stages III and IV), one complete remission and four partial regressions were achieved. Five patients are still alive after 6 to 14 mo. In 15 non-Hodgkin lymphoma patients, 2 complete remissions and 7 partial regressions were achieved. Eight patients are still alive after 4 to 12 mo. Severe toxicities related to the chemotherapy protocol have never been observed. These results demonstrate the efficiency of the described chemotherapy schedules in advanced malignant lymphomas resistant to usual therapy. (Author abstract) (15 Refs) (In FRE)

MALIGNANT LYMPHOMA: MULTIMODAL THERAPY

36. PAEDIATRIC NON-HODGKIN'S LYMPHOMAS: THE CHILDREN'S CANCER STUDY GROUP EXPERIENCE. AN INTERIM REPORT.

Jenkin RD, Anderson JR, Chilcote RR, Coccia P, Exelby P, Kersey J, Kushner J, Meadows A, Siegel S, Wilson J, Leiken S, Hammond D
Dept. Radiology, Univ. Toronto, Ontario Cancer Foundation, Toronto-Bayview Clinic, 2075 Bayview Ave., Toronto, Ontario, M4N 3M5, Canada
Front Radiat Ther Oncol; 16:134-140 1982

Children in the nonleukemic stages of non-Hodgkin's lymphomas (NHL) were given combination chemotherapy for 18 mo, standardized radiotherapy (max, 3,000 rads for local vol, 2,000 rads whole-abdomen), and intrathecal (ith) methotrexate (MTX: days 5, 31, and 34 of induction, then every 28 days). Some patients were randomized to the LSA2-L2 regimen of induction (37-day course) with cyclophosphamide (CP), vincristine (VCR), MTX (iv and ith), prednisone (PRN), and daunomycin (DNM); consolidation (about 7 wk) with cytosine arabinoside (ara-C), 6-thioguanine (TG), L-asparaginase, MTX (ith), and carmustine (BCNU); and maintenance (every 28 days) with cycles of TG-CP, hydroxyurea-DNM, MTX (po)-BCNU, ara-C-VCR, and ith MTX. The other patients were given the COMP regimen (27-day induction, maintenance every 28 days) of CP, VCR, MTX (ith and iv), and PRN. In the total group (374 patients), the 3-yr survival rate was 66% and the relapse-free survival (RFS) rate was 61%. In 118 patients with localized NHL, the 3-yr RFS rates were comparable with LSA2-L2 (81%) and COMP (85%). In 256 patients with nonlocalized NHL, the outcome depended on tumor histology. The 3-yr RFS rate in lymphoblastic NHL was 73% with LSA2-L2 and 31% with COMP. The 2-yr RFS rate in non-lymphoblastic NHL was higher with COMP than with LSA2-L2 in diffuse histiocytic NHL (69% vs 26%), Burkitt-type diffuse undifferentiated NHL (64% vs 20%), and pleomorphic diffuse undifferentiated NHL (59% vs 29%). In the total group, about 5% died of toxicity during remission and 7% developed isolated first CNS relapses. Most relapses developed within 2 yr. The optimal treatment of childhood NHL is not yet clear, but these results showed that histology-specific chemotherapy can be curative in about 70% of children with nonlocalized NHL. (8 Refs)

37. NON-HODGKIN'S PRIMARY MALIGNANT LYMPHOMAS OF THE DIGESTIVE TRACT.

Diebold J, Audouin J, Auffret Y, Balouet G, Barjou B, Bataille F, Belz L, Ben Bouali A, Bertrand G, Bonard J, Borel B, Bouc M, Boutiller J, Briere J, Bruel M, Bretagne JF, Caron-Poitreau C, Cazagou JF, Dartois M, Dauver A, David P, Jacob J, Jobard P, Josso A, Davy A, Joubaud F, Justum AM, Lancien G, Laroche C, Delmas P, Launois B, Le Bodic L, Le Bodic MF, Leguene B, Delorme B, LemevelB, L'Hintre M, L'Hirondel C, Louvet M, Derobert L, Mandard P, Marchand P, Marionneau J, Metman EH, Dhermies J, Mo
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Ann Gastroenterol Hepatol; 18(2):97-113 1982

A retrospective study of 60 cases of non-Hodgkin's malignant lymphomas of the digestive tract revealed that epigastric pain and changes in patient's general health were the most common symptoms on presentation. In 7/13 cases examined endoscopically, there were obvious malignant ulceration of the stomach. Tumors classified as highly malignant (35) outnumbered those less invasive (17). There were 16 tumors larger than 5 cm. Surgery with curative intent was performed in 88% of the cases. Palliative surgery was most often performed when the small intestine (4/28) was involved. Postsurgical mortality (PM) was 11.5%. PM was a function of patient's age, health status, and type of surgery. Radiotherapy and chemotherapy, alone or associated, completed surgical treatment in 37 cases. Thirty-three patients survived between 1-6 yr, and 27 died after a period of a few mo to 2 yr. The overall survival rate at 1 yr was 60%. Of the 37 patients who received adjuvant therapy, 19 (51%) were alive after 1 yr with no apparent recurrence. Only 6/16 (37%) of the patients who did not receive complementary treatment were alive after 1 yr. (48 Refs) (In FRE)

38. NON-HODGKIN'S LYMPHOMA IN THE GASTROINTESTINAL TRACT.

Melsom H, Rode L, Kaalhus O, Elgjo RF, Langholm R, Marton P
Alminnelig avdeling, Det Norske Radiumhospital, Montebello, Oslo 3, Norway
Tidsskr Nor Laegeforen; 102(6):374-377 1982

Primary non-Hodgkin's lymphoma of the gastrointestinal tract was diagnosed in 61 patients. Lymphosarcoma was found in 20 patients, reticulosarcoma in 32 and unclassifiable lymphoma in 9. According to the Kiel classification, lymphocytic lymphoma was diagnosed in 2 patients, lymphoplasm cytoid lymphoma in 22, centrocytic lymphoma in 2, centroblastic/centrocytic lymphoma in 18, lymphoblastic lymphoma (including Burkitt's lymphoma) in 8, immunoblastic lymphoma in 4, and unclassifiable lymphoma in 4. Pains, weight loss, emesis and nausea were the most frequent symptoms. The disease was diagnosed in most patients within 3 mo from the onset of the first symptoms The tumor was localized in the stomach in 31 patients, in the small intestine in 15, in the large intestine in 5, in the ileocecal region in 4, and in the mesentery in 6. Thirty patients were in Stage I, 31 in II. Eleven patients (10 in Stage I and 1 in II) were subjected to surgery only, 19 (including 10 in Stage I) to surgery and radiotherapy, 31 (including 10 in Stage I) to surgery, radiotherapy and cytostatic therapy. The 5-yr survival rate was higher than 60% for the patients with gastric lymphomas, but lower than 25% for those with tumors of other localization in the intestine. The 3-yr survival rate was 9/11 after surgery only. The 5-yr survival rate was 13/19 after surgery with postoperative radiotherapy and 3/31 after surgery with radiotherapy and cytostatic therapy. Surgery with postoperative radiotherapy was found to be most effective in patients with limited disease. (10 Refs) (In NOR)

39. PRIMARY NON-HODGKIN'S LYMPHOMAS OF THE STOMACH. REPORT OF 18 CASES. THE VALUE OF FIBROSCOPY AND DISCUSSION OF THERAPEUTIC APPROACH.

Sondag D, Baumann R, Lacroute J, Schutz J, Bergerat J, Weill-Bousson, Weill J
Service de Gastroenterologie, CHU de Strasbourg, Hopital de Hautepierre, F67098 Strasbourg, France
Ann Gastroenterol Hepatol; 18(2):115-123 1982

Radiographic examination of 18 cases of primary malignant non-Hodgkin's stomach lymphomas, indicated malignancy in 12 cases, and diffuse modifications in 2 cases. The radiologic anomalies were localized 16x. Fibroscopic examination revealed definite malignant lesions in 15 cases and suspected malignancy in 3 cases. In 13/18 cases malignancy was confirmed by biopsies. In addition, the diagnosis of malignant lymphoma could be established in five cases even though it was not possible to determine the exact histological type. In seven cases, there was ganglionic abdominal involvement which was confirmed by laparotomy and biopsy. All patients underwent surgical treatment with some form of gastrectomy in 17 cases. Adjuvant chemotherapy was used in eight cases and two patients were also treated with radiotherapy. The two patients who died within 6 mo of surgery had an immunoblastic form of lymphoma. For the six patients who survived at least 4 yr, the histological types of lymphoma were centrocytic (3), lymphocytic (1), and centroblastic (2). (36 Refs) (In FRE)

MALIGNANT LYMPHOMA: CASE REPORTS

40. TUBULAR COMPLEXES OF ENDOPLASMIC RETICULUM IN LYMPHOBLASTIC LYMPHOMA: CASE REPORT.

Chu H, Foucar K, Barlogie B, Middleman E
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Cancer; 49(8):1629-1635 1982

Distinctive intracytoplasmic tubular complexes have been identified occasionally by electron microscopy in a wide variety of hematologic and nonhematologic disorders. The mechanism of induction and significance of these tubular complexes are unknown. Tubular complexes were identified in the majority of bone marrow lymphoma-leukemia cells in a patient with documented lymphoblastic lymphoma in lymph node. These complexes varied in size but in general ranged from 800-1,500 nm, and consisted of masses of nonparallel, twisted, smooth, 40-nm tubules. Continuity with adjacent endoplasmic reticulum was evident in some of the complexes. Cytochemical characteristics of the malignant cells included strong, focal, paranuclear acid phosphatase reactivity and strong, stippled nuclear terminal deoxynucleotidyl transferase positivity. Flow cytometric analysis showed a DNA-RNA content pattern consistent with acute lymphoblastic leukemia and typical of T-cell lymphoma. This represents the first report of such tubular complexes in a presumed T-cell malignancy. (Author abstract) (33 Refs)

41. NONCUTANEOUS PERIPHERAL T-CELL LYMPHOMA HISTOLOGICALLY RESEMBLING MYCOSIS FUNGOIDES.

Weisenburger DD, Nathwani BN, Forman SJ, Rappaport H
Dept. Pathology, Mercy San Juan Hosp., 6501 Coyle Ave., Carmichael, CA, 95608
Cancer; 49(9):1839-1847 1982

We have studied the clinical and pathologic features of three patients with a distinctive non-Hodgkin's lymphoma of the diffuse mixed cell type. The tumors were characterized by a mixture of lymphoid cells of widely varying size and degree of nuclear transformation. A distinctive feature of the neoplastic cells was the presence of cerebriform nuclear contours identical to those seen in mycosis fungoides. Immunologic studies performed on lymph nodes from two patients revealed that the neoplastic cells were T-cells. Characteristic clinical features of the patients were an advanced stage of disease at diagnosis, absence of skin lesions, presence of lung involvement, poor response to aggressive chemotherapy, and a short survival time (9-13 mo). The features described closely resemble those of the pleomorphic variant of Japanes adult T-cell leukemia-lymphoma. (Author abstract) (44 Refs)

MALIGNANT LYMPHOMA: SELECTED REPORTS ON ETIOLOGY AND EPIDEMIOLOGY

42. FINAL CASE REPORTING FROM THE UGANDAN PROSPECTIVE STUDY OF THE RELATIONSHIP BETWEEN EBV AND BURKITT'S LYMPHOMA.

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International Agency Res. Cancer, 150 Cours Albert Thomas, 69372 Lyon, France
Int J Cancer; 29(4):397-400 1982

A prospective epidemiological study was carried out in the West Nile District of Uganda from 1972 to 1979 in order to investigate the etiological role of the Epstein-Barr virus (EBV) in Burkitt's lymphoma (BL). By 1976, 14 BL cases had been detected among the 42,000 children originally bled in the study area. Testing of sera from BL candidates and neighborhood controls showed that children who develop BL later have EBV/VCA titers several dilutions higher than their age- and sex-matched neighbors. This appearance of a strong EBV activity long before BL development was taken as evidence of a causal role of EBV in BL in order to add to the unique material of pre-bled BL cases, BL detection was continued up to March 1979 when field work became impossible in Uganda. Two additional pre-bled BL cases were found during this extension of the study. The serological and virological evaluation of these additional cases showed that the EBV/VCA titers, but not the EA and EBNA titers, were about two dilutions higher in the BL candidates than in the controls. Hybridization assays showed that both lymphomas contained EBV/DNA in the tumor cells. These additional results thus confirm the findings in the first 14 cases and strengthen the epidemiological evidence for a causal role of the EBV in endemic BL. (Author abstract) (10 Refs)

43. NATURAL ANTIBODIES TO THE STRUCTURAL CORE PROTEIN (P24) OF THE HUMAN T-CELL LEUKEMIA (LYMPHOMA) RETROVIRUS FOUND IN SERA OF LEUKEMIA PATIENTS IN JAPAN.

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Proc Natl Acad Sci USA; 79(5):1653-1657 1982

We investigated the involvement (in adult T-cell leukemias and lymphomas) of the human T-cell leukemia virus (HTLV) that was previously isolated in one of our laboratories from cultured T cells of some patients in the United States with leukemias and lymphomas involving relatively mature T cells. High titers of antibodies capable of quantitative precipitation of 125I-labeled p24, a well characterized core protein of HTLV, were detected in 12 of 12 patients with untreated adult T-cell leukemia (ATL). (1 negative was a patient on chemotherapy). Ten of the 12 positive samples were from an area where the disease is endemic. Strong precipitating antibodies were also detected in five of seven cases of T-cell malignant lymphoma (TML) which differs from ATL by having fewer leukemic cells in the peripheral blood. High antibody titers were also observed in one of five cases of acute monoblastic leukemia and one of eight cases of chronic myelogenous leukemia in the blast phase of the disease. Low to moderate titers of antibodies were detected in several categories of leukemia (2 cases of blast-phase chronic myelogenous leukemia, 2 cases of acute lymphoblastic leukemia of the null-cell type, and 1 case of acute myelogenous leukemia). Among all categories of leukemias, except ATL and TML, more cases were negative than positive for anti-p24 activity. All of 79 sera from normal Japanese, including 39 collected from the endemic ATL area of southwest Japan, were negative for antibodies to HTLV p24. All the positive reactivities observed were highly specific to HTLV. The only competition observed in the precipitation of HTLV p24 was with HTLV or with cell lines expressing HTLV and not with various animal retroviruses or a large number of human and subhuman primate cell lines, not known to be producing HTLV. The data strongly indicate an association of HTLV with the increased incidence of ATL in parts of Japan, probably with other forms of leukemias in Japan, and, less commonly, with certain T-cell malignancies in the United States. (26 Refs)

44. DEVELOPMENT OF MALIGNANT LYMPHOMA IN MYOEPITHELIAL SIALADENITIS (SJOGREN'S SYNDROME).

Schmid U, Helbron D, Lennert K
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Virchows Arch [Pathol Anat]; 395(1):11-43 1982

Forty-five cases of myoepithelial sialadenitis (MESA) were investigated histologically, immunologically, and clinically. Two patients with clinical evidence of Sjogren's syndrome were also included in the study, though salivary gland biopsies showing MESA were not available. A total of 16 patients had Sjogren's syndrome or another type of autoimmune disease. In 42 cases of MESA, so-called proliferation areas composed of immunoblasts and lymphoplasmacytoid cells were found. The proliferation areas were small and circumscribed in 16 cases, and extensive and confluent in 26 cases. All the confluent proliferation areas analyzed with the immunoperoxidase (PAP) method showed a monotypic immunoglobulin pattern (predominantly IgM/K). Extrasalivary malignant lymphoma with the same histologic and immunohistologic features as the confluent proliferation areas was found in 14 patients. Thus, this type of MESA is called 'manifest malignant lymphoma'. The tumor was classified as LP immunocytoma in 23 patients, and as LP immunocytoma transforming into immunoblastic lymphoma in three patients. One patient developed nodal B-immunoblastic lymphoma. The term 'early lymphoma' is suggested for MESA with circumscribed proliferation areas showing a monotypic immunoglobulin pattern (usually IgM/K), because extrasalivary malignant lymphoma developed later in four of the patients with this type of MESA. The two patients with only clinical evidence of Sjogren's syndrome also showed extrasalivary malignant lymphoma (LP immunocytoma in 1 case and immunoblastic lymphoma in the other). There is a close histogenetic relation between MESA with or without autoimmune disease and certain malignant non-Hodgkin's lymphomas of B type, namely, LP immunocytoma and B-immunoblastic lymphoma. The interval between the appearance of salivary gland enlargement and the diagnosis of malignant lymphoma varied from 1.5 to 12 yr. Generalization of malignant lymphoma led to death in 11 cases. (Author abstract) (113 Refs)

45. PSEUDOLYMPHOMAS OF THE OCULAR ADNEXA: THEIR RELATIONSHIP TO SJOGREN'S SYNDROME.

Dhermy P, Diebold J, Audoin J, Tricot G
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J Fr Ophtalmol; 4(12):787-796 1981

Of 15 cases of Sjogren's syndrome, there were nine lacrimal localizations and seven pseudolymphomas. All patients were women with an av age of 51 yr. The ocular involvement was marked by hypertrophy of the lacrimal glands in eight cases, by lacrimal hyposecretion associated with hypertrophy in two cases and by isolated hyposecretion in one case. The lesions are described as a non-malignant lymphoproliferation or a pseudolymphoma which is between glandular localization of Sjogren's syndrome and neoplasia. In most cases, immunofluorescent studies revealed polyclonal secretions with a predominance of IgM. Because of this hyperplasia of B lymphocytes which is at first polyclonal and then capable of becoming monoclonal, the pseudolymphomas should be considered precancerous and treated accordingly. Immunosuppressive therapy using chlorambucil or cyclophosphamide has produced excellent results and is preferred to radiotherapy which has been thought to favor malignant transformation in some cases. (27 Refs) (In FRE)

46. TONSILLECTOMY, APPENDECTOMY AND MALIGNANT LYMPHOMAS.

Silingardi V, Venezia L, Tampieri A, Gramolini C
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Scand J Haematol; 28(1):59-64 1982

According to some authors, prior tonsillectomy and/or appendectomy increase the frequency of certain types of neoplasm. Seven-hundred thirty-one cases of malignant lymphoma, Hodgkin's disease (HD) and non-Hodgkin lymphoma (NHL), and an equal number of controls were reviewed retrospectively to evaluate the frequency of tonsillectomy and appendectomy and the age at onset of the lymphomas. The results exclude that prior tonsillectomy and/or appendectomy increase the probability of development of lymphomas. Likewise, the age at onset of HD or NHL was not influenced by the surgical ablation of the palatine tonsils and the appendix. (Author abstract) (33 Refs)

47. VARIABLY ACID-FAST PLEOMORPHIC BACTERIA AS A POSSIBLE CAUSE OF MYCOSIS FUNGOIDES. A REPORT OF A NECROPSIED CASE AND TWO LIVING PATIENTS.

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J Dermatol Surg Oncol; 8(3):203-213 1982

Variably acid-fast coccoid forms, morphologically suggestive of acid-fast, cell-wall deficient mycobacteria, were found within sections from a fatal case of mycosis fungoides and from two living patients with the disease. The autopsy case was a 52-yr-old man who died after a 9-yr history of mycosis fungoides and a 1-yr history of lymphocytic lymphoma. Acid-fast coccoid forms were detected throughout most of the autopsy material, both in histologically normal and abnormal sections of tissues including the myocardium, lungs, lymph node, liver, intestinal wall, kidney, adrenals, parathyroid gland, prostate, and connective tissue. Acid-fast coccoid forms also were seen in biopsy specimens of the lymph node and skin taken 1 yr antemortem. Numerous blood cultures had been negative, except one that showed Pseudomonas maltophilia, which was regarded as a contaminant. Numerous skin biopsies taken from the other two patients showed intra- and extracellular, variably acid-fast coccoid forms. (39 Refs)

MALIGNANT LYMPHOMA: SELECTED PRE-CLINICAL STUDIES

48. SUPPRESSION OF SPONTANEOUS LYMPHOMA BY PREVIOUSLY UNDISCOVERED DOMINANT GENES IN CROSSES OF HIGH- AND LOW-INCIDENCE MOUSE STRAINS.

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Virology; 118(1):76-85 1982

Crosses of mice of the high-lymphoma mouse strains, AKR and C58, with mice of the low-lymphoma strains, C57L, DBA/1, and DBA/2, produce F1 generations with low and late incidences of the spontaneous disease. Backcross populations, obtained from high-lymphoma parental strain x low-lymphoma F1 matings, showed lymphoma incidences of approx 75%, indicating that the low lymphoma incidence in F1 mice of these crosses was due to the simultaneous presence of at least two independently segregating dominant genes inherited from the low-lymphoma parental strain. In none of the three crosses was lymphoma resistance linked to the Fv-1 locus, and in only one (AKR x C57L) was H-2 type a significant determinant of the disease. This finding indicates that previously undiscovered genes possess the capacity to suppress spontaneous murine lymphoma. Studies of the expression of endogenous ecotropic and xenotropic murine leukemia viruses in mice of these crosses suggest that one of the new genes involved in lymphoma suppression may act by delaying the expression of xenotropic virus. (Author abstract) (25 Refs)

49. VIRUS CLONED FROM THE RAUSCHER VIRUS COMPLEX INDUCES ERYTHROBLASTOSIS AND THYMIC LYMPHOMA.

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Virology; 118(1):225-228 1982

The pathogenicity of two ecotropic viruses cloned from a Rauscher virus complex (RV), that had been passaged in the mouse, has been studied. One of the viruses, R-MuLV, gives rise to syncytia in the XC test (XC-positive), the other, R-XC-virus, does not (XC-negative). Both cloned viruses induce erythroblastosis and thymic lymphoma after inoculation into newborn NIH Swiss mice. Another clonal isolate of R-MuLV, from a stock which has been propagated in tissue culture, similarly induces both diseases when injected into newborn NIH Swiss mice. All R-MuLV and R-XC- induced splenic and thymic tumors produced, in addition to the injected virus, mink cell focus-inducing virus. This is consistent with the idea that MCF viruses are the actual (proximal) viruses causing the proliferative processes in the hematopoietic cells which lead to the different diseases. The finding that an R-MCF virus, which in most cases induces erythroblastosis, can also induce thymic lymphoma at a low frequency suggests that both diseases could be induced by the same MCF virus. (Author abstract) (18 Refs)

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
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HE 20.3173/2:

HODGKIN'S DISEASE: DIAGNOSIS AND STAGING

1. TRIAL OF CORRELATING THE LYMPHOGRAPHIC FINDINGS WITH MORPHOLOGICAL PATTERN IN PATIENTS WITH HODGKIN'S DISEASE.

Zaborowski Z
Zaklad Rentgenodiagnostyki, Wojewodzki Szpital Zespolony, Al. Niepodleglosci 15 m. 89, 02-653 Warsaw, Poland
Nowotwory; 31(3/4):199-205 1981

Correlations between the lymphographic pattern and histological type of Hodgkin's disease (HD) were studied in 118 patients (71 men and boys and 47 women and girls, av age 40.5 yr) with HD. Lymphocyte predominant (LP) type was diagnosed histologically in 32 patients, nodular sclerotic (NS) type in 44, mixed cellular (MC) type in 34 and lymphocyte depleted (LD) type in 8. The LP type was characterized lymphographically by underlining of marginal sinuses, blurred structure of nodes and vesicular clearings of varying size, while the LD type featured partial filling of marginal sinuses causing blurring of lymph node contours and filling defects of varying size. Fairly sharply outlined filling defects of varying shapes, lack of filling of marginal sinuses at the site of filling defects, and distention of certain marginal sinuses of straight course were seen in the NS type. The lymph nodes resembled homogeneous structure with small filling defects with rather blurred borders in the MC type. The lymphographic pattern was suggestive of a given histological type in 49.15% of all cases: the correlation between the lymphographic pattern and histological type was 43.75% for the LP type, 52.27% for the NS type, 52.94% for the MC type and 37.50% for the LD type. (21 Refs) (In POL)

2. THE CHANGING ROLE OF STAGING LAPAROTOMY IN HODGKIN'S DISEASE: A PERSONAL SERIES OF 310 PATIENTS.

Glees JP, Barr LC, McElwain TJ, Peckham MJ, Gazet JC
Royal Marsden Hosp., Sutton, Surrey, England
Br J Surg; 69(4):181-187 1982

A series of 310 patients with Hodgkin's disease having a staging laparotomy under the care of one surgeon between October 1969 and June 1980 is presented. A total of 51% had positive laparotomy findings, and 30% had their staging altered, but there was a low incidence of positive laparotomy findings when performed within 2 mo of initial treatment by chemotherapy. None of the investigations used to determine possible splenic or hepatic involvement preoperatively was found to be of any value, and their routine use is not recommended. Bipedal lymphography was found to give an accurate assessment of iliac and lower para-aortic nodal involvement, and so the laparotomy protocol since 1975 has not included biopsy of these nodes. The incidence of minor complications was 31% and of major complications 4%. One patient died. Staging laparotomy has played an important part in the management of Hodgkin's disease over the past decade, but it is likely to assume a less prominent role in the 1980s as the role of chemotherapy in early Hodgkin's disease expands. In nonbulky clinical Stage I and II Hodgkin's disease, when radiotherapy alone is curative, then a staging laparotomy is justifiable because it will detect occult abdominal disease, especially in the lymphogram-negative patient, which may require the addition of chemotherapy or more extensive radiotherapy. Laparotomy is essentially an operation to remove the spleen and to obtain adequate liver biopsy specimens in order to ascertain possible involvement of these two organs. Non-opacified nodes at the porta hepatis and coeliac axis should also be sampled, as should a node from the poorly opacified upper paraaortic area. Routine oophoropexy is not recommended. (Author abstract) (17 Refs)

3. STAGING LAPAROTOMY IN HODGKIN'S DISEASE. MAYO CLINIC EXPERIENCE.

Martin JK, Clark SC, Beart RW, ReMine WH, White WL, Ilstrup DM

Mayo Clinic, 200 First St. SW, Rochester, MN, 55905

Arch Surg; 117(5):586-591 1982

Between 1967 and 1979, 316 patients with Hodgkin's disease underwent staging laparotomy. Histologic examination demonstrated lymphocyte predominance in 40 (12.7%) patients, nodular sclerosis in 178 (56.3%), mixed cellularity in 80 (25.3%), and lymphocyte depletion in 7 (2.2%); results in 11 (3.5%) patients were considered unclassifiable. There were no deaths. Major complications occurred in 7.9% and required reoperation in 1.9%. Pathologic stage differed from clinical stage in 111 (35.1%) patients. In 90 (28.5%) patients, the stage advanced; in 21 (6.6%) patients, the stage was reduced; and in 5 (1.6%) patients, the histologic subtype was changed. Stage changes occurred in 40% of those with lymphocyte predominance, in 27.5% with nodular sclerosis, in 46.3% with mixed cellularity, and in 85.7% with lymphocyte depletion. The reliability of staging laparotomy for the determination of appropriate treatment favors its continued use. (Author abstract) (21 Refs)

4. SURGICAL STAGING OF HODGKIN'S DISEASE: CONSIDERATIONS AFTER 10 YEARS EXPERIENCE.

Saba V, Chan R, Braccioni U

Insegnamento di Chirurgia Sperimentale, Universita di Ancona, Ancona, Italy

Minerva Med; 73(15):935-938 1982

Ninety two patients [52 with Hodgkin's lymphoma (HL), 9 with non-Hodgkin's lymphoma, 5 with leukemia, and others] underwent splenectomy. Surgical procedure included splenectomy, hepatic biopsy of each lobe with Menghini's needle, examination and biopsy of the lymph nodes, ovariopexy in young women, and iliac bone marrow biopsy. Of the 52 patients (27 men, 25 women; 10-70 yr old, most of them 30-50 yr old), 35 had nodular sclerosis, 8 had predominance of lymphocytes, 5 had depletion of lymphocytes, and 5 had mixed cellularity. None of the patients showed hepatic, and only 13 had splenic involvement. Before surgery, 16 of the patients were in Stage I, 33 were in Stage II, 5 were in Stage III, and 1 was in Stage IV. After surgery, 10 were in Stage I, 19 were in Stage II, and 22 in Stage III. Surgical complications included embolism in one of the patients, dehiscence of wound in three, and infections in six, but without surgical mortality. Splenectomy is a valid method in the diagnosis and staging with low morbidity and absence of mortality. (16 Refs) (In ITA)

HODGKIN'S DISEASE: CLINICAL IMMUNOLOGY AND IMMUNOTHERAPY

5. DISTRIBUTION OF T-LYMPHOCYTE SUBSETS IN HODGKIN'S DISEASE CHARACTERIZED BY MONOCLONAL ANTIBODIES.

Dorreen MS, Habeshaw JA, Wrigley PF, Lister TA
ICRF Dept. Medical Oncology, St. Bartholomew's Hosp., West Smithfield, London EC1A 7BE, England
Br J Cancer; 45(4):491-499 1982

Mononuclear-cell suspensions of lymph nodes, spleen and blood from 24 patients with active Hodgkin's disease (HD) were studied for possible imbalance of T and B lymphocytes, and T-lymphocyte subsets, using monospecific anti-T antibodies and other reagents. A profile showing T-cell predominance was demonstrated in lymph nodes and blood, with total T-cells ranging from 50-70% of the cell count. As defined by monoclonal antibodies, 70-85% of the latter comprised the 'inducer' subclass, the remainder being 'suppressor' cells. There were no essential differences between histologically involved and uninvolved lymph nodes from HD patients, though total T-cell proportions were lower in 'normal lymph node' controls. The profiles of spleens electively removed, as part of pretreatment staging procedures, showed reduced total T-cell numbers, whether these were involved with HD or not. These differences are accounted for principally by fewer T 'inducer' cells (24%, in spleen, vs 54% in involved lymph nodes and 47% in 'normal' control nodes). Possible explanations for these findings are discussed. Our results demonstrate similar profiles in histologically diseased and normal tissue, rather than any clear imbalance of T-cell proportions which might explain the profound disturbances of T-cell function frequently demonstrated in vivo and in vitro. (Author abstract) (41 Refs)

6. NONSPECIFIC IMMUNE RESPONSE IN HODGKIN'S DISEASE.

Rytwinski K, Schneiberg K, Szelc S, Kolosza Z, Tabenska J
Oddzial w Gliwicach, Instytut Onkologii, ul Wybrzeze Armii Czerwonej 15, 44-101 Gliwice, Poland
Nowotwory; 31(3/4):181-190 1981

The nonspecific immunity was investigated in 58 patients (31 men and 27 women, 17-69 yr old) with Hodgkin's disease before treatment. Stage I according to the Ann Arbor Classification was established in 6 patients, II in 25, III in 18 and IV in 9. The histological classification revealed lymphocyte predominance in 7 patients, nodular sclerosis in 28, mixed cellularity in 18 and lymphocyte depletion in 5. The IgA, IgG and IgM levels were significantly increased and the percentage T cells was reduced in the entire group compared with 25 healthy controls. The absolute total lymphocyte count, lymphotoxin activity, phytohemagglutinin-induced blast transformation, and the percentage of positive dinitrochlorobenzene (DNCB) skin tests were reduced significantly. The decrease in the functional efficiency of the lymphocytes in the blast transformation tests, in the lymphotoxin activity, and the impairment of the response to DNCB were most pronounced in the patients in Stages III and IV, which suggests a positive correlation of these parameters with the clinical course of the disease. Positive correlation was found between the results of the DNCB skin test and blast transformation. A drastic decrease of both parameters was observed in the patients with lymphocyte predominance and the reduction of the T cell count was greatest in the patients with mixed cellular type. (30 Refs) (In POL)

HODGKIN'S DISEASE: CHEMOTHERAPY

7. ETOPOSIDE AS A SINGLE AGENT IN RELAPSED ADVANCED LYMPHOMAS: A PHASE II STUDY.

Taylor RE, McElwain TJ, Barret A, Peckham MJ
Inst. Cancer Res., Royal Marsden Hosp., Downs Road, Sutton Surrey, England
Cancer Chemother Pharmacol; 7(2/3):175-177 1982

Twenty-three patients (22-69 yr old) with relapsed lymphomas resistant to conventional chemotherapy were treated with VP16-213 in a Phase II study. Thirteen patients had Hodgkin's disease (HD) and 10 had non-Hodgkin's lymphoma (NHL). VP16-213 was administered at 120 mg/square meter iv daily for 5 days or po for 7-10 days, repeated at 3-wk intervals. Of 12 evaluable patients with HD (1 patient died of progressive disease), complete remission occurred in 3 and partial remission in 5; three partial remissions were observed in the 9 evaluable patients with NHL. Major toxicity was hematologic (anemia, leukopenia, thrombocytopenia); infection due to neutropenia occurred in five patients. All patients experienced some nausea and alopecia. At high dosage levels, VP16-213 was particularly effective (61%) in HD. (12 Refs)

HODGKIN'S DISEASE: RADIOTHERAPY

8. ABNORMAL HEAT SIZE AND FUNCTION AFTER RADIATION (RT) TO THE MEDIASTINUM IN PATIENTS (PTS) WITH HODGKIN'S DISEASE (MEETING ABSTRACT)

Gomez GA, Bakshi S, Krishnamsetty RM, Park JJ, Parthas KL, Henderson E
Roswell Park Memorial Institute, Buffalo, NY, 14263
Proc Am Soc Clin Oncol; 1:C-607 1982

Changes in the heart structures produced by RT of the mediastinum are reported to be temporary and of no clinical significance in the majority of pts. We compared the transverse diameter of the heart (TDH) and the cardiothoracic ratio (C/T) on PA chest x-rays before treatment and at last follow-up in 70 pts with Hodgkin's disease ranging in age 20 to 51 years who received RT to the mediastinum (3600 rads) as part of their initial treatment. Thirty-three had RT as the only treatment, 37 had RT plus chemotherapy (CT) either initially or as salvage treatment. All 70 were in complete remission (CR) with a median follow up of 66 months after onset of therapy. A decrease in TDH of 1 to 3.5 cm was observed in 22/23 pts treated with RT (66%) and in 26/37 treated with RT + CT (70%). Mean decrease of TDH was 1.8 cm in both groups. Decrease in C/T ratio ranging from 0.1 to 0.11 was observed in 26 patients treated with RT and 27 treated with RT + CT. Ejection fraction (EF) by radionuclide cine angiocardiograms was measured in 17 pts. EF ranged from 31 to 77% normal greater than or equal to 55%. Low normal or abnormal EF was observed in pts with little or no decrease in TDH or C/T, but were more profoundly abnormal in those with marked decreases in TDH or C/T. None of these pts has overt heart failure or constrictive pericarditis. (no Refs)

HODGKIN'S DISEASE: MULTIMODAL THERAPY

9. ABVD CHEMOTHERAPY IN THE TREATMENT OF HODGKIN'S DISEASE.

Bonadonna G, Santoro A
Istituto Nazionale Tumori, Via Venezian, 1, 20133 Milan, Italy
Cancer Treat Rev; 9(1):21-35 1982

The most important therapeutic and toxicologic results observed with adriamycin, bleomycin, vinblastine, and dacarbazine (ABVD) are analyzed and some practical conclusion as to the optimum use of this drug regimen in the treatment of Hodgkin's disease (HD) are presented. Rationale for ABVD combination is presented. Essential therapeutic results of ABVD-treatment in 54 mechlorethamine, vincristine, procarbazine, and prednisone (MOPP)-resistant patients are summarized. The most important finding was that 32 of 54 patients (59%) achieved complete remission (CR). The likelihood of CR was significantly influenced by the absence of extranodal disease and of systemic symptoms. A number of MOPP-salvage programs were developed. The most important current regimens and their results are summarized. Seventy-five consecutive patients with initial Stage IV HD (55 patients) or extranodal relapse following primary radiotherapy (20 patients) were randomly allocated to receive either 12 cycles of MOPP or MOPP monthly alternated with ABVD for total of 12 cycles. Results indicate that the cyclical delivery of two non-cross-resistant combinations offers a promise for higher CR rate, longer duration of relapse-free survival (RFS), and hopefully higher cure rate of advanced HD compared to the continuous administration of the classical MOPP alone. Comparative results of MOPP-radiotherapy-MOPP treatment (75 patients) vs ABVD-radiotherapy-ABVD treatment (78 patients) are summarized. ABVD plus radiotherapy appears more effective than MOPP plus radiotherapy in terms of CR, particularly in patients with nodular sclerosis, large mediastinal adenopathy and B symptoms, as well as in RFS of Stage III HD. The comparative toxic effects of ABVD vs MOPP are reviewed. (42 Refs)

10. STAGE I AND II HODGKIN'S DISEASE: INVOLVED-FIELD RADIOTHERAPY VERSUS EXTENDED-FIELD RADIOTHERAPY VERSUS INVOLVED-FIELD RADIOTHERAPY FOLLOWED BY SIX CYCLES OF MOPP.

Hagemeister FB, Fuller LM, Velasquez WS, Sullivan JA, North L, Butler JJ, Johnston DA, Shullenberger CC
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Cancer Treat Rep; 66(4):789-798 1982

Results of laparotomy treatment in staged patients with Stage I or II Hodgkin's disease were investigated in 90 patients treated by involved-field (IF) radiotherapy, 65 by extended-field (EF) radiotherapy, and 41 by IF plus MOPP chemotherapy [mechlorethamine, vincristine (oncovin), prednisone, and procarbazine; 6 cycles]. Of the 196 evaluable patients, 101 had mediastinal disease and 95 did not. Five-yr survival rates were 94% for patients treated with IF, 94% for those treated with EF, and 98% for those treated with IF + MOPP. However, the 5-yr disease-free survival rates were 90% for those treated with IF + MOPP, 72% with IF alone, and 66% with EF. Patients without mediastinal disease had better survival results than those who had mediastinal involvement at presentation. Pathology appeared to have no effect on treatment results of patients treated with radiotherapy alone. Patients with large mediastinal disease tended to relapse most often in the thoracic area, those without mediastinal disease relapsed most often in nonirradiated nodes of the upper and lower torso. Treatment of relapsed patients was more successful when the relapse was in a nodal area not previously treated with radiotherapy. Few complications of therapy occurred, and chemotherapy was well tolerated by most patients. These findings were used to construct a treatment plan for patients with Stage I or II Hodgkin's disease. (27 Refs)

11. TREATMENT OF ADVANCED HODGKIN'S DISEASE: 10-YEAR EXPERIENCE IN THE EASTERN COOPERATIVE ONCOLOGY GROUP.

Glick JH, Barnes JM, Bakemeier RF, Prosnitz LR, Bennett JM, Neiman RS, Costello W, Orlow EL
Hematology-Oncology Section, Hosp. Univ. Pennsylvania, 3400 Spruce St., Philadelphia, PA, 19104
Cancer Treat Rep; 66(4):855-870 1982

Between 1972 and 1981, the Eastern Cooperative Oncology Group completed two major studies of advanced Hodgkin's disease. The first trial, EST 2472, demonstrated that the five-drug combination of carmustine (BCNU), cyclophosphamide, vinblastine, procarbazine, and prednisone (BCVPP) is an effective alternative to mechlorethamine, vincristine, prednisone, and procarbazine (MOPP) chemotherapy. Although the complete remission (CR) rate for BCVPP (77%) was similar to that for MOPP (73%) in this randomized trial, the choice of induction chemotherapy significantly influenced CR duration. Patients achieving CR with BCVPP had a significantly greater disease-free survival than those who achieved CR with MOPP (65% vs 50%, respectively, at 5 yr, $p = 0.02$). Overall survival is not different at this time between patients who received BCVPP and those who received MOPP. BCVPP produced significantly less gastrointestinal toxicity and neurotoxicity than MOPP. There was no influence on CR duration or survival with maintenance chemotherapy or BCG immunotherapy when compared to no further treatment. In the second trial, EST 1476, there was only a 58% CR rate with six cycles of low-dose bleomycin-MOPP induction chemotherapy. Complete responders and continuing partial responders were then randomized to receive either non-cross-resistant chemotherapy with doxorubicin, bleomycin, vinblastine, and DTIC (dacarbazine) (ABVD) or low-dose radiotherapy to all sites of pretreatment involvement except bone marrow. Fifty percent of the partial responses were converted to CR with either ABVD or radiotherapy consolidation. The overall Cr rate at the end of consolidation was 68%. At the present time, there is no significant difference in disease-free or overall survival between ABVD and radiotherapy. (Author abstract) (19 Refs)

12. COMBINED MODALITY THERAPY FOR ADVANCED HODGKIN'S DISEASE: LONG-TERM FOLLOW-UP DATA.

Prosnitz LR, Farber LR, Kapp DS, Bertino JR, Nordlund M, Lawrence R
Dept. Therapeutic Radiology, Yale Univ. Sch. Medicine, 333 Cedar St., New Haven, CT, 06510
Cancer Treat Rep; 66(4):871-879 1982

From 1969 to 1979, 155 patients with advanced Hodgkin's disease were treated with a combined modality protocol (combination chemotherapy and irradiation to all sites of disease). The actuarial 10-yr survival of all patients who started therapy is 78%, and the relapse-free survival is 67%. Within the group of patients with advanced disease, age greater than 40 yr and/or Stage IV disease with multiple extranodal sites of involvement adversely affected prognosis. Since 1978, these patients have been treated with chlormethine, vincristine, procarbine and prednisone (MOPP)-ABVD and irradiation, with a resulting 3-yr survival of 87% compared with 58% for those treated with mechlorethamine, vincristine, vinblastine, procarbazine and prednisone (MVVPP) in prior years. A comparison between MVVPP and MOPP, also begun in 1978, has thus far yielded no significant differences. Second malignancies have occurred in four patients apparently cured for their Hodgkin's disease: two patients with acute leukemia and two with non-Hodgkin's lymphoma. Avascular necrosis of bone has developed in nine patients. There have not been other serious long-term complications. This combined modality treatment approach appears to offer a significant survival advantage compared with treatment programs using chemotherapy alone. (Author abstract) (27 Refs)

13. EFFICACY OF RADIATION (RT) PLUS COMBINATION CHEMOTHERAPY (CT) VS RT OR CT ALONE FOR SELECTED SUBGROUPS IN HODGKIN'S DISEASE (HD) (MEETING ABSTRACT)

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Fitzsimons Army Medical Center, Aurora, CO, 80045
Proc Am Soc Clin Oncol; 1:C-610 1982

The treatment of 186 consecutive patients (pts) seen at FAMC between 1968 and 1979 with HD were reviewed. Pts with stage IB and IIB treated with RT vs RT + CT had a 100% complete response (CR) rate with either treatment. Five of 8 patients in the RT alone group relapsed compared to 0/7 relapses in the RT + CT group. Salvage therapy with CT achieved a CR in 80% of relapses with no significant difference in survival at a median follow-up (F/U) of 83 mo. Eighteen of 25 (72%) of stage IIIB and IV pts treated with CT achieved a CR vs 7/7 pts treated with RT + CT. There was a trend favoring overall survival in the RT + CT group with a median F/U of 37 months in pts with CR. RT included at least involved fields in all RT + CT groups. From the above data we conclude that: 1) A high relapse rate in IB and IIB pts treated with RT alone when combined with incomplete salvage rates would tend to support combined RT + CT as initial therapy to minimize relapses, despite lack of significant survival difference. 2) The trend in CR rate and survival favors RT + CT vs CT alone in pts with advanced HD (IIIB and IV). (no Refs)

HODGKIN'S DISEASE: CASE REPORTS

14. A CASE OF HODGKIN'S DISEASE OF THE SMALL INTESTINE AND REVIEW OF REPORTED CASES IN JAPANESE LITERATURE.

Yagita A, Miura S, Shinoda M, Kimura T, Hosoda Y, Shiina E, Higuchi T
Dept. Surgery, Saitama Chuo Hosp., Urawa, Japan
I To Cho; 16(10):1061-1066 1981

A case of lymphocytic depletion-type Hodgkin's disease that occurred in a 72-yr-old man with complaints of abdominal pain and a palpable mass was reported. Based on laboratory findings, double-contrast roentgenography, endoscopy, and biopsy, malignant lymphoma was suspected and a curative right hemicolectomy was performed. Histopathological examination of the surgical specimen showed invasion of tumor cells into the serosal layer of the terminal portion of the ileum and in 2/8 regional lymph nodes. Seven other cases of Hodgkin's disease of the small intestine have been reported in Japan, but this is the only case that was (1) discovered with roentgenography of the cecum and endoscopy and (2) was diagnosed preoperatively as malignant lymphoma. (26 Refs) (In JPN)

15. THE OPHELIA SYNDROME: MEMORY LOSS IN HODGKIN'S DISEASE.

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Lancet; 1(8276):844-845 1982

Memory loss of recent events was diagnosed as part of a paraneoplastic syndrome in a 16-yr-old girl with Hodgkin's disease. The patient presented with progressive loss of memory of recent events, depression, and hallucinations. Chest x-ray and mediastinoscopy revealed a large lung mass. Hodgkin's disease was diagnosed and treated with radiotherapy and chemotherapy. Memory was restored with the exception of an 18-mo gap. The concomitant appearance of memory loss and Hodgkin's disease is discussed. (1 Ref)

MALIGNANT LYMPHOMA: DIAGNOSIS AND STAGING

16. NATIONAL CANCER INSTITUTE SPONSORED STUDY OF CLASSIFICATIONS OF NON-HODGKIN'S LYMPHOMAS. SUMMARY AND DESCRIPTION OF A WORKING FORMULATION FOR CLINICAL USAGE.

Non-Hodgkin's Lymphoma Pathologic Classification Project, Rosenberg SA, Berard CW, Brown BW, Burke J, Dorfman RF, Glatstein E, Hoppe RT, Simon R, Henry K, Lennert K, Lukes RJ, O'Conor G, Rappaport H, Hartsock R, Kruger G, Nanba K, Robb-Smith AH, Sacks M, Banfi A, Bloomfield C, Bonadonna G, DeLellis R, DeVita VT, Frizzera G, Hu MS, Kaplan HS, Rilke F, Rosai J, Rudders RA, Warnke RA, Ziegler JL
(c/o Rosenberg) Div. Oncology, S-025, Stanford Univ. Sch. Medicine, Stanford, CA, 94305
Cancer; 49(10):2112-2135 1982

An international multi-institutional clinicopathologic study of 1,175 cases of non-Hodgkin's lymphoma sponsored by the National Cancer Institute has been completed. Histologic slides and clinical records were examined from previously untreated patients seen during the period between July 1971 and December 1975 at four institutions, three in the United States and one in Italy. The reproducibility and clinical relevance of the six major classifications of the non-Hodgkin's lymphomas was tested by six 'expert' pathologists, each a proponent of a major classification, and six very experienced pathologists not identified with one of the major classifications. Immunologic methods were not employed in the study design. A summary of the methods employed and the conclusions of the study is described. The major conclusion was that all six classifications were valuable and comparable in reproducibility and clinical correlations. The clinical significance of a follicular architecture, independent of cell type was confirmed. A working formulation of non-Hodgkin's lymphomas is described which separates the disease into 10 major types utilizing morphologic criteria only. Subtypes are also described which allow translation of all of the major classifications into comparable groups. Histologic criteria are presented for each major type and equivalent terms are given for each type in the six major classifications. The formation is not proposed as a new classification but a means of translation among the various systems and to facilitate clinical comparions of case reports and therapeutic trials. The report contains commentaries by five of the 'expert' pathologists on the value and conclusions of this unique study. (Author abstract) (48 Refs)

17. LYMPHOMA IN CARDIAC ALLOTRANSPLANT RECIPIENTS. CLINICAL AND HISTOLOGICAL FEATURES AND IMMUNOLOGICAL PHENOTYPE.

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Transplantation; 33(4):347-351 1982

To characterize further lymphomas which arise in chronically immunosuppressed allotransplant patients, we studied the clinical and histological features of seven cases of nonHodgkin's lymphoma and determined the immunological phenotype in four cases, which developed in a series of 182 patients who underwent cardiac transplantation at Stanford University Hospital. Clinical features which were correlated with the development of lymphoma included patient age, pretransplant diagnosis, and the number of transplants. All cases of non-Hodgkin's lymphoma presented as solitary or multiple localized extranodal lesions while none presented in lymph nodes. Extranodal sites of involvement included brain, lung, and soft tissues of the thigh at the site of antilymphocyte serum injections. Histologically, five of seven lymphomas were classified as high grade, large cell, immunoblastic and two of seven as intermediate grade, large noncleaved cell. The immunological phenotype of the neoplasm from four patients was determined by reaction with immunoglobulin light and heavy chain reagents and monoclonal antibodies to T cell and B cell antigens. All lymphomas from four patients which were tested stained for Ia antigen (HLA-DR) but did not stain for immunoglobulin or the T cell antigens detected in this study. (Author abstract) (33 Refs)

18. CYTOGENETICS OF MALIGNANT LYMPHOMAS.

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Dtsch Med Wochenschr; 107(12):468-471 1982

Methods and findings of cytogenetic analysis of malignant lymphomas (ML) are reviewed. Analysis consists of counting and structural examination of chromosomes using fluorescence or Giemsa banding techniques. Specific abnormalities characteristic of ML include loss or gain of certain chromosomes, presence of specific chromosomal alterations, and increased frequency of rearrangements of specific chromosomal regions. The most common extra chromosomes found in lymphomas are chromosomes 7, 3, and 12. The most common structural change is the marker 14q+, found in 64% of all lymphomas. Epstein-Barr virus (EBV) apparently is linked to chromosome 14, although the 14q+ marker is also found in EBV-negative lymphomas. Chromosome 14 is apparently involved in control of cell proliferation. Other chromosomes frequently showing alterations in lymphomas are 1, 6, and 11. Chromosome 1 is of particular importance in myeloid lymphomas. Chromosomal rearrangement alters gene function by a position effect. ML cells show a rate of sister chromatid exchange double of that found in normal cells, indicating chromosomal instability. Cytogenetic analysis can be used to differentiate ML from other lymphatic disorders. Staging of ML is aided by detection of chromosomal abnormalities in otherwise apparently normal biopsy tissue. Presence or absence of particular anomalies is of prognostic value, especially in cases of B-cell acute lymphatic leukemia and hairy-cell leukemia. (18 Refs) (In GER)

19. PRIMARY MALIGNANT LYMPHOMA OF THE BRAIN - A COMPARATIVE STUDY WITH SYSTEMIC LYMPHOSARCOMA.

Nakanishi I, Kono K, Kubota T, Tsuchiya Y, Kitamura T, Masuda S, Moriizumi T
Dept. Pathology, Sch. Medicine, Kanazawa Univ., Kanazawa, Japan
No Shinkei Geka; 10(1):35-42 1982

Five cases of primary malignant lymphoma of the brain were presented and the comparison between malignant lymphoma of the brain and different types of systemic lymphosarcoma was made in terms of morphological features of their tumor cells by light and electron microscopies. It was found that the tumor cells of primary malignant lymphoma of the brain were similar to those of systemic lymphosarcoma on the basis of their histology, histochemical properties and ultrastructure. Cell origin of the tumor cells and clinical aspects of primary malignant lymphoma of the brain were further discussed. (Author abstract) (24 Refs) (In JPN)

20. NATURAL HISTORY OF LYMPHOID LESIONS OF THE ORBIT AND CONJUNCTIVA (MEETING ABSTRACT)

Robert NJ, Silberman N, Pilch BZ, Harris N, Goodman ML
Departments of Pathology and Ophthalmology, Massachusetts Eye and Ear Infirmary, Boston, MA
Proc Am Soc Clin Oncol; 1:C-746 1982

The findings are reported of a retrospective review of 67 cases of lymphoid infiltration of the orbit or conjunctiva seen at the Massachusetts Eye and Ear Infirmary from 1955 to 1975. Cases were reviewed by two independent panels of observers, histopathological diagnoses were compared, and diagnostic criteria established. There were 43 cases of infiltration of the orbit and 24 cases of infiltration of the conjunctiva. Diagnoses were benign lymphoid infiltrate (48/67), atypical lymphoid infiltrate (7/67), and lymphoma (12/67). The most common lymphoma type was poorly differentiated lymphocytic lymphoma (5/11), and the dominant site was the orbit (10/11). Forty-three cases were further evaluated with a median follow-up of nine years. In this group patients with lymphoma often presented with initial lesion in the orbit with subsequent dissemination. Three of 5 patients with atypical lymphoid infiltrates and 5/29 patients with benign lymphoid infiltrate had a prior history of lymphoma or subsequently developed lymphoma. In summary, a twenty-year experience at a large referral hospital reveals that only a minority of lymphoid infiltrates of the orbit or conjunctiva represent lymphoma. The majority of cases were diagnosed as benign lymphoid infiltrations. However, a small number of patients in this latter group, and especially patients with atypical lymphoid infiltrates, had lymphoma or subsequent diagnosis of lymphoma. (no Refs)

21. MALIGNANT LYMPHOMA OF THE THYROID GLAND: A CLINICOPATHOLOGIC STUDY.

Kapadia SB, Dekker A, Cheng VS, Desai U, Watson CG
Dept. Pathology, Presbyterian-Univ. Hosp., DeSoto at O'Hara St., Pittsburgh, PA, 15213
Head Neck Surg; 4(4):270-280 1982

A total of 21 cases of thyroid lymphoma diagnosed during a 12 yr period (1969-1980) is reviewed. The most common presenting symptoms were a rapidly growing thyroid mass with hoarseness, dysphagia, and breathing difficulty. The thyroid was the primary site in 19 patients, and thyroid lymphoma was part of systemic involvement in 2 patients. The 20 non-Hodgkin lymphoma patients had a mean age of 66 yr, 75% were women, and all were Caucasian. Most patients had diffuse histiocytic lymphomas. Hashimoto thyroiditis was associated in 57% of the patients. Intracytoplasmic monoclonal immunoglobin was present in five of 15 cases. All 21 patients underwent surgery, 19 received radiotherapy, and 13 chemotherapy. Fourteen patients are dead. The overall median survival was 8 mo. The remaining six patients are alive and free of disease for 9-68 mo (mean: 27 mo). The major cause of death was dissemination after local control by radiotherapy. Median survival was longer in men, patients under 65 yr of age, and patients who did not have extrathyroid soft tissue or regional lymph node involvement. The histologic features that aid in the differential diagnosis of malignant thyroid lymphoma are discussed. (32 Refs)

22. COMPUTED TOMOGRAPHY OF GASTRIC LYMPHOMA.

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(c/o Moss) Dept. Radiology, M-396, Univ. California, Sch. Medicine, San Francisco, CA, 94143
AJR; 138(5):859-865 1982

The CT features in 12 patients with gastric lymphoma, 4 primary and 8 secondary, were analyzed, correlated with other diagnostic studies, surgery, and pathologic features, and compared with the CT findings in 22 patients with gastric adenocarcinoma. An abnormally thickened gastric wall (mean, 4.0 cm) was found in all patients with gastric lymphoma. Lymphomas of the stomach often involved more than one region of the stomach (83%). The contour of the outer gastric wall, was smooth or lobulated in 42%, perigastric lymph adenopathy was common (58%), extension into adjacent organs was found in 42%, and 42% had lymphadenopathy at or below the renal pedicle. (Author abstract) (34 Refs)

23. SERUM FERRITIN AND BONE MARROW HAEMOSIDERIN IN PATIENTS WITH MALIGNANCIES AND IN HEALTHY CONTROLS.

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Scand J Haematol; 28(3):264-271 1982

Serum ferritin has been analyzed and bone marrow hemosiderin evaluated in 306 patients with malignancies, mostly lymphomas, and in 46 healthy controls. Also hemoglobin, serum iron, transferrin and liver enzymes were analyzed simultaneously. Sixty percent of the patients had serum ferritin above normal values and 20% had values above 1,000 ug/l. There was a good correlation between serum ferritin and bone marrow iron both in the patients and in the controls, $r = 0.67$ and $r = 0.77$, respectively. There was a negative correlation between serum ferritin and hemoglobin concentration in the patients and a positive correlation in the controls. In patients with Hodgkin's disease serum ferritin was related to the stage of the disease. (Author abstract) (19 Refs)

MALIGNANT LYMPHOMA: CLINICAL IMMUNOLOGY AND IMMUNOTHERAPY

24. OBJECTIVE REGRESSIONS OF T- AND B-CELL LYMPHOMAS IN PATIENTS FOLLOWING TREATMENT WITH ANTI-THYMOCYTE GLOBULIN.

Fisher RI, Silver BA, Vanhaelen CP, Jaffe ES, Cossman J
NIH, NCI, Building 10, Room 12N226, 9000 Rockville Pike, Bethesda, MD, 20205
Cancer Res; 42(6):2465-2469 1982

We have conducted a clinical trial utilizing anti-thymocyte globulin (ATG) for the treatment of patients with non-Hodgkin's lymphomas. Six patients were treated; 50% reductions in tumor mass of short duration were observed in one patient with a T-cell lymphoma and two patients with B-cell lymphomas. In vitro assays have been performed in an attempt to study the reactivity and potential mechanisms of antitumor action of the ATG. The ATG bound to essentially all normal blood mononuclear leukocytes as well as tumor cells from patients with T-, B-, or null cell lymphomas demonstrating its lack of specificity. Furthermore, complement-mediated lysis of normal mononuclear leukocytes, normal T- or B-cells, and tumor cells from two unresponsive patients were all comparable; moreover, since this lysis occurred only at concentrations of ATG that are not attainable in vivo, it is unlikely that complement-mediated cytotoxicity accounts for the responses observed. Peripheral blood lymphocyte counts and total erythrocyte rosettes did decrease during ATG treatment. Thus, objective tumor responses in both B- and T-cell non-Hodgkin's lymphomas can be achieved with a very nonspecific antiserum although significant toxicity resulted. Whether the magnitude or duration of response can be increased with monoclonal antibodies remains to be determined. Future success with serotherapy might require use of either a battery of different monoclonal antibodies or a single monoclonal antibody that can deliver radioisotopes, chemotherapy, or toxins to the tumor cells. (Author abstract) (13 Refs)

25. DEFICIENT HELPER T CELL ACTIVITY IN NON-HODGKIN'S LYMPHOMAS (MEETING ABSTRACT)

Silver BA, Bostick-Bruton FW, Young RC, Fisher RI
Medicine Branch, National Cancer Institute, Bethesda, MD, 20205
Proc Am Assoc Cancer Res; 23:991 1982

The observations that lymphomas are more common 1) after organ transplantation and immunosuppressive therapy, and 2) in certain autoimmune diseases suggest that altered immunoregulation may play a role in lymphoma pathogenesis. Thus, we investigated regulatory T cell function in the peripheral blood in 13 untreated adult non-Hodgkin's lymphoma patients and 13 age and sex matched controls. Six patients had nodular lymphomas, 7 diffuse. Nine had B cell tumors. No known T cell tumors were studied. Control mononuclear leukocytes (MNL) had greater proliferative responses to pokeweed mitogen (PWM) than patient MNL. MNL were separated into T and non-T fractions by two sequential neuraminidase-E-rosette sedimentations. Non-T cells were unresponsive to PWM. Responses of normal and patient T cells were similar. When normal non-T and autologous irradiated (3000R) T cells were cocultured, the response exceeded the response of patient non-T and autologous irradiated T cocultures. When normal non-T cells were cocultured with patient irradiated T cells, their response was diminished. Moreover, when patient non-T cells were cocultured with normal irradiated T cells, their response was enhanced. Normal non-T cell responses were the same regardless of whether autologous or normal allogeneic irradiated T cells were used as helpers. These results suggest that peripheral blood T cells from patients with non-Hodgkin's lymphoma are deficient in helper capacity for non-T cell blastogenic response to PWM and that patient non-T cells may have a normal proliferative response in the presence of normal allogeneic (helper) T cells. Abnormal immunoregulatory cell function may be important in the pathogenesis of the non-Hodgkin's lymphomas. (no Refs)

26. HELPER T-CELL FACTOR IN SERUM FROM PATIENTS WITH NON-HODGKIN'S MALIGNANT LYMPHOMAS (MEETING ABSTRACT)

Chartrand SL, Gajl-Peczalska KJ
University of Minnesota, Minneapolis, MN, 55455
Fed Proc; 41(3):335 1982

T cell fraction (mean 97% E-rosette forming cells) was obtained from peripheral blood of healthy volunteers. T cells were cultured separately for 5 days with 50% serum from 13 newly diagnosed patients with non-Hodgkin's malignant lymphomas, 50% serum from allogeneic normal control donors and 50% fetal calf serum (FCS). T cells were then mixed with allogeneic tonsillar B lymphocytes, stimulated with pokeweed mitogen, and after 12 day cultures the IgA, IgG and IgM secretion was measured by double-antibody radioimmunoassay. It was found that the serum from approximately 70% patients with B cell lymphomas enhanced helper T cell function when compared to serum from normal individuals. The highest enhancing effect, expressed as a n-fold increase of Ig secretion with T cells precultured in patient versus control serum, was found in IgG production; it was somewhat lower for IgA, and the lowest for IgM. Ig secretion with T cells precultured with FCS was generally lower than with control human serum. Therefore the values calculated against T lymphocytes precultured in FCS were slightly higher, the mean for IgG being 9.8, for IgA 6.6 and for IgM 5.3. The attempts to characterize the enhancing factor present in the serum of lymphoma patients will be presented. (no Refs)

27. MONOCLONAL AND HETEROLOGOUS REAGENTS IN THE PHENOTYPING OF LYMPHOMAS (MEETING ABSTRACT)

Barcos M, Minato K, Minowada J, Han T, Henderson E, Ozer H
Roswell Park Memorial Institute, Buffalo, NY, 14263
Proc Am Assoc Cancer Res; 23:1008 1982

Nodal and extranodal biopsies from 34 patients with malignant lymphoma were tested for E total, E gravity, EA, EAC, and heterologous anti-TLCL, c-ALL, Ia, K and lambda reagents. Selected cases were also tested with nine reagents for T-cell subsets (Leu 1, 2a, 3a, 4; OKT 3, 4, 6, 8, 11A). There were 27 B cell (21 K, 6 lambda), 6 T-cell and 1 undefined cell lymphomas. Study of frozen sections by the biotin-avidin immunoperoxidase or immunofluorescence method was essential for the accurate analysis of 5/9 follicular small cleaved B, 2/2 diffuse cerebriform T and 4/4 diffuse mixed or large T-cell lymphomas. The c-ALL 'early lymphoid differentiation' antigen was detected in 4/17 (23%) cases tested, including 2 follicular small cleaved B, 1 diffuse small cleaved B, and 1 diffuse mixed T-cell lymphomas. The Ia-like antigen was detected in 22/24 (92%) B-cell and in 3/6 (50%) T-cell lymphomas tested. E gravity was significantly increased in 1/6 T-cell lymphomas to 49%. The six T-cell lymphomas consisted of one case with 'helper-inducer' (Leu 3a, OKT 4) phenotype, one case with 'suppressor-cytotoxic' (Leu 2a, OKT 8) phenotype, and four cases with a mixed 'helper-suppressor' cell phenotype. (no Refs)

28. PLATELET ASSOCIATED IGG IN PATIENTS WITH LYMPHOMA (MEETING ABSTRACT)

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Proc Am Soc Clin Oncol; 1:C-31 1982

Thrombocytopenia and platelet-associated IgG(PAIgG) have been described in association with Hodgkin's (HD) and non-Hodgkin's lymphoma (NHL). To estimate the incidence of PAIgG in patients (pts) with these disorders, 49 consecutive pts with HD or NHL seen at this Center were screened for PAIgG using a modification of the platelet radioactive antiglobulin test of Mueller-Eckhardt. Nine of 20 pts (45%) with HD and 9/29 pts (31%) with NHL had positive assays. Pts with HD and PAIgG tended to have lower platelet counts (PC) than those with HD and negative PAIgG. There appeared to be a higher incidence of thrombocytopenia during the course of treatment in pts with HD and PAIgG. All pts with HD and PAIgG had advanced stage and all were nodular sclerosing or mixed cellularity subtypes. In HD, PAIgG was not independently predictive of active disease (8/9 PAIgG positive and 7/11 PAIgG negative pts had active disease). PAIgG became negative, however, in 4 pts on treatment. In pts with NHL, PAIgG correlated with active disease and occurred exclusively in the poor prognostic categories. There was no difference in PC between PAIgG positive and negative pts with NHL. Hypergammaglobulinemia was not related to increased PAIgG. This study indicates an unrecognized high incidence of PAIgG with lymphoma. (no Refs)

29. DEMONSTRATION OF OKT 6-REACTIVE CELLS IN MYCOSIS FUNGOIDES.

McMillan EM, Beeman K, Wasik R, Everett MA

Dept. Dermatology, Univ. Oklahoma Health Science Center, Oklahoma City, OK

J Am Acad Dermatol; 6(5):880-887 1982

Dermal and epidermal lymphoid infiltrates of five patients with mycosis fungoides (MF), plaque stage (3), tumor stage (2), were examined for the presence of OKT 6-reactive cells using the indirect immunoperoxidase technique. Numerous OKT 6-positive cells were identified in the dermis in all patients. The cells tended to be interspersed throughout the infiltrates and were present in superficial and deep layers of dermis. The overall percentage of OKT 6-reactive cells was approx 5-10% of the infiltrating population. The staining pattern observed often appeared dendritic but to varying degrees throughout infiltrates. In all patients numerous positive-staining cells were observed in the epidermis, and these often appeared to have dendritic staining pattern. In three patients who had shown numerous Pautrier microabscesses, OKT 6-positive cells were often identified with Pautrier abscesses and were occasionally found to lie at the periphery of the abscess but formed only a component of it, mainly negatively staining cells being seen. The staining pattern in these cells was also dendritic. The results in the positive control of thymus showed positive staining of a population which was predominantly cortical in location. The results confirmed that OKT 6-reactive cells may be found outside the thymus. (35 Refs)

30. COMPLEMENT (C3) RECEPTORS ON DENDRITIC RETICULUM CELLS OF NORMAL AND MALIGNANT LYMPHOID TISSUE.

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Clin Exp Immunol; 48(2):348-352 1982

The aim of this study was to investigate whether dendritic reticulum cells (DRC) in normal lymphoid tissue and in malignant non-Hodgkin's lymphomas possess receptors for the third complement component (C3 receptors). For this purpose we studied the in situ expression of C3 receptors in lymphoid tissue by staining frozen tissue sections with an antiserum specific for human C3 receptors (AC3RS), using a modified immunoperoxidase method. The results indicate that DRC of normal and malignant lymphoid tissue express large amounts of C3 receptors. Absorption experiments revealed that the C3 receptors of DRC are identical with, or at least share common antigenic sites with, the C3 receptors expressed by tonsil B cells. (Author abstract) (17 Refs)

31. IN SITU IDENTIFICATION OF LANGERHANS CELLS IN THE DERMAL INFILTRATE OF CUTANEOUS T CELL LYMPHOMA.

Chu A, Berger CL, Kung P, Edelson RL
(c/o Edelson) Dept. Dermatology, Coll. Physicians and Surgeons, Columbia Univ., 630 West 168th St., New York, NY, 10032
J Am Acad Dermatol; 6(3):350-354 1982

Skin biopsies from 28 patients with cutaneous T-cell lymphomas (CTCL, mycosis fungoides: 23/28), cutaneous metastases from B-cell lymphomas (BL: 2/28), or benign lymphocytoma cutis (BLC) were assayed using monoclonal antibodies reacting against Langerhans cells (LC) and cross-reacting with T- or B-lymphocytes, helper T-cells, or monocytes/histiocytes. None of the biopsied areas had been exposed to local or systemic treatment. In 22/23 CTCL biopsies, a minor (up to 5%) but significant proportion of the CTCL cells showed the LC surface phenotype, together with the phenotype of helper T-cells. No T-cell antigens were identified. Since the BL and BLC biopsies lacked cells having the LC surface phenotype, their presence in CTCL suggested that this neoplasm may be a T-cell neoplasm. (25 Refs)

32. IN SITU IMMUNOLOGIC PHENOTYPING OF MYCOSIS FUNGOIDES.

McMillan EM, Wasik R, Beeman K, Everett MA
Dept. Dermatology, Univ. Oklahoma Health Science Center, Oklahoma City, OK
J Am Acad Dermatol; 6(5):888-897 1982

In situ analysis of mycosis fungoides (MF) infiltrates with the use of monoclonal antibodies directed against T cells and T cell subsets in conjunction with the indirect immunoperoxidase technique is described. Punch biopsies were taken from six patients with MF. Two patients were affected by tumor stage MF and the remainder by plaque stage. The specificity and source of antibodies used are presented. In one patient with MF plaque stage, weak reactivity was observed with peripheral T cell antibodies, Leu 1, and OKT 3, in approx 50% of the cells. In three patients with plaque stage MF and one with tumor stage MF, a significant component of the dermal infiltrates (greater than or equal to 50%) was found to react positively with peripheral T cell antibodies Leu 1 and OKT 3. The results in the dermis with 'helper' antibodies Leu 3A and OKT 4 also indicated that a significant component of the populations reacted positively with these antibodies. Testing of the dermal infiltrates with 'suppressor' antibodies Leu 2 and OKT 8 gave a negative reaction in one patient and a positive reaction in a small number of cells in three patients. The majority of cells in the Pautrier abscesses stained positively with the peripheral T cell antibodies. Analysis with 'helper' antibodies gave a positive reaction in many of the cells constituting the abscesses. Testing with the 'suppressor' antibodies gave a negative reaction in the Pautrier abscesses in all three patients. Results in the positive control of tonsil were positive with all primary antibodies, with a predominantly interfollicular distribution of positive-reacting cells. Results with Leu 1 and OKT 3 indicate that a significant component of cutaneous infiltrating mononuclear cells of MF react with antibodies which normally detect mature T cell antigens. (33 Refs)

MALIGNANT LYMPHOMA: CHEMOTHERAPY

33. METHYL-GLYOXAL BIS-GUANYLHYDRAZONE (METHYL-GAG) IN THE MANAGEMENT OF NON-HODGKIN'S LYMPHOMA (NHL) (MEETING ABSTRACT)

Kuhn JG, Knight WA, McDaniel TM, Coltman CA, Whitecar JP, Fabian C, Costanzi JJ
University of Texas Health Science Center, San Antonio, TX, 78284
Proc Am Soc Clin Oncol; 1:C-635 1982

A total of 21 refractory patients with histologically proven NHL ((diffuse, well differentiated (diff, well)-7; diffuse, poorly differentiated (diff pdl)-3; diffuse, histiocytic-4; diffuse convoluted-1; nodular poorly differentiated-3, and nodular mixed (nod, mixed)-3) (M/F: 15/6; median age 61 (30-73)) were treated with an initial dose of Methyl-GAG of 600 mg/m2 in D5W over 30 minutes. This was followed by weekly infusions with 50 mg/m2 increments in the absence of toxicity. When toxicity was reached, treatment was given every other week. Moderate (6) to severe (4) nausea and vomiting was the most common toxicity, mucositis (3) and severe leukopenia and thrombopenia (2) were less common. Patients had failed a median of 8 drugs prior to Methyl-GAG (Range 4-11) and 11/21 had failed prior radiotherapy. Five of 21 (diff, well-2/7; diff, pdl-1/3; nod, mixed-2/3) achieved partial response ranging from 2+ to 52 weeks. Methyl-GAG is active in NHL and further patient accrual is needed to test its true activity in the various histological classifications. In addition, 2 of 2 patients with stage IV mycosis fungoides achieved partial responses lasting 4 and 53 weeks. (no Refs)

34. VM 26 IN NON-HODGKIN LYMPHOMA (NHL) EFFECTIVENESS ACCORDING TO WORKING FORMULATION (WF) GRADE OF MALIGNANCY, PRIOR TREATMENT AND AGE (MEETING ABSTRACT)

Tirelli U, Galligioni E, Frustaci S, Longhi S, Carbone A, Veronesi A, Roncadin M, Grigoletto E, Tumolo S, Trovo MG, Zagonel V, Canale VC, Frgoli F
Division of Radiotherapy and Medical Oncology, General Hospital of Pordenone, 33170 Pordenone, Italy
Proc Am Soc Clin Oncol; 1:C-637 1982

The purpose of the study was to determine the effectiveness of VM 26 in NHL according to WF grade of malignancy, prior treatment and age. VM 26 100 mg/m2 iv was given for at least 3 cycles to 49 consecutive NHL patients (pts), either failures after conventional therapy or previously (prev) untreated (untr) elderly (greater than 65 yrs) pts. VM26 was most effective in intermediate-high grade malignancies and in elderly prev untr pts. The treatment was very well tolerated even by the elderly pts. Our preliminary conclusions are: 1) VM 26 is a very effective drug in elderly prev untr pts, with 44% of sustained CR (median duration of 18+ weeks), 2) in pts with WF low grade of malignancy, a lesser response to VM 26 is expected. (no Refs)

35. THE TREATMENT OF MYCOSIS FUNGOIDES WITH OINTMENT-BASED MECHLORETHAMINE.

Price NM, Deneau DG, Hoppe RT
Dept. Dermatology, Mycosis Fungoides Clinic, Stanford Univ. Medical Center, Stanford, CA, 94305
Arch Dermatol; 118(4):234-237 1982

The use of topical mechlorethamine hydrochloride in the treatment of skin disease has been restricted because of the frequent development of contact dermatitis. A series of 24 patients with mycosis fungoides in Stages 1A (8 patients), 1B (15 patients), and 2 (1 patient) were treated with ointment-based mechlorethamine, prepared by an anhydrous method. This preparation was therapeutically effective. Complete clearing occurred in 15 of 18 patients with active disease over evaluation periods of up to 27 mo, and one patient had partial clearing. Two patients showed a partial relapse during their evaluation periods. The incidence of contact dermatitis was very low: 8% in individuals with a history of hypersensitivity to mechlorethamine and 0% in patients being exposed to the medication for the first time. This new preparation has been shown to be effective therapy for mycosis fungoides. Patient use is associated with minimal side effects. (Author abstract) (18 Refs)

MALIGNANT LYMPHOMA: RADIOTHERAPY

36. HOME ULTRAVIOLET PHOTOTHERAPY OF EARLY MYCOSIS FUNGOIDES: PRELIMINARY OBSERVATIONS.

Milstein HJ, Vonderheid EC, Van Scott EJ, Johnson WC
(c/o Vonderheid), Skin and Cancer Hosp., 3322 North Broad St., Philadelphia, PA, 19140
J Am Acad Dermatol; 6(3):355-362 1982

UV phototherapy at home was given to 34 patients (20 men, 14 women; median, 52 yr old) with parapsoriasis en plaques (PEP: 3/34) or early mycosis fungoides (MF: 31/34). The MF patients showed slowly progressive disease of long duration (10 to greater than 25 yr in 18/31) and no signs of extracutaneous dissemination. Clinically complete remissions (CR) were obtained in 2/3 PEP and 29/31 MF patients, after 1-10 mo of UV treatment. Five patients did not respond after 3-6 mo of UV treatment, which was discontinued. At least 7/34 patients did not follow the recommended protocol (daily until CR, then every other day) and 4/7 showed only partial responses. UV treatment was intentionally stopped in 11 MF patients, to assess the duration of unmaintained CR. Four patients continued maintenance treatment for 3-7 mo after the beginning of CR; all relapsed after 4-8 mo off treatment, but showed another CR when UV treatment was resumed. Seven patients continued maintenance UV treatment for 11-19 mo after the beginning of CR; one patient relapsed (5 mo of treatment) and the others continued in CR (4-20 mo of treatment). All patients who continued UV treatment remained in CR at the time of report (3-30 mo, median greater than 18 mo). The decision to continue UV treatment after the beginning of an apparent clinical CR was supported by the evidence of persistent MF in repeat biopsies from 5/18 patients in apparent CR. The other biopsies showed histologic evidence of mild chronic dermatitis. The adverse effects of home UV treatment were minimal. Although other treatment modalities may achieve a higher CR rate, UV phototherapy may be indicated for selected MF patients. Controlled trials of conventional phototherapy in MF patients are recommended. (20 Refs)

MALIGNANT LYMPHOMA: MULTIMODAL THERAPY

37. RANDOMIZED COMPARISON OF CHOP VS BLEO-CHOP FOR THE TREATMENT OF DIFFUSE NON-HODGKIN'S LYMPHOMA (NHL) (MEETING ABSTRACT)

Koziner B, Kurland E, Little C, Thaler H, Labriola D, Lee BJ, Straus DJ, Kempin S, Mertelsmann R, Arlin Z, Hansen H, Nisce L, Clarkson BD
Memorial Sloan-Kettering Cancer Center, New York, NY, 10021
Proc Am Soc Clin Oncol; 1:C-625 1982

Seventy-nine patients (pts) with stages II (10), IIE (4) III (17) and IV (48) of diffuse lymphocytic poorly differentiated (20), diffuse histiocytic (DHL) (49) and other (10) lymphomas were treated on the NHL-5 protocol. This program compared by randomization 8 cycles of CHOP (cyclophosphamide, vincristine doxorubicin at 50 mg/m2 and prednisone) versus 8 cycles of CHOP preceded by Bleomycin iv at 20 mg/m2 in continuous infusion for 5-7 days in cycles 1 and 5. After completion of chemotherapy, radiotherapy was given to areas of initial bulky disease. Intrathecal Methotrexate was administered to all pts with bone marrow involvement. Of the 79 pts, only 66 were evaluable for response to therapy. The overall response rate was 91% with 62% in complete remission (CR) and 29% in partial remission (PR). Of the 33 pts that received CHOP, 26 achieved a CR (79%) and 6 a PR (18%). Only 1 failure was observed. Seven relapses occurred in pts that achieved a CR (27%) and 4 in pts that achieved a PR (65%). Of the 33 pts that received Bleo-CHOP, 15 achieved a CR (45%), 13 a PR (39%) and 5 failed to respond. Four relapses occurred in pts that achieved a CR (27%) and 6 in pts that achieved a PR (46%). The significant difference in CR rate between CHOP and Bleo-CHOP was partly explainable by higher serum LDH (lactic dehydrogenase) levels in the latter arm. Although pts with B symptoms and prior chemotherapy were also more common in the Bleo-CHOP arm, they did not explain the persistent difference in CR rate among stage IV DHL patients. (no Refs)

38. DIFFUSE HISTIOCYTIC LYMPHOMA (DHL) WITH SCLEROSIS AND PRIMARY MEDIASTINAL INVOLVEMENT: AN ENTITY RESISTANT TO THERAPY (MEETING ABSTRACT)

Miller JB, Variakojis D, Sweet DL, Golomb HM, Ultmann JE
The University of Chicago, Chicago, IL, 60637
Proc Am Soc Clin Oncol; 1:C-626 1982

Of 170 patients with DHL seen at the University of Chicago, 31 (18%) were classified as having moderate to marked sclerosis. Nine of the 31 (29%) had predominantly retroperitoneal nodal masses and six others had involvement in various other sites outside the mediastinum, including bone with (2) or without (1) nodal disease, localized peripheral nodal (1), testicular (1), or widespread nodal involvement (1). Sixteen of the

31 patients (52%) had bulky disease seen predominantly or exclusively in the mediastinum. Of these 16, four were in Pathologic Stage (PS) IIA, nine were in Clinical Stage (CS) II, two were in CS III, and one was in PS IV on the basis of pleural fluid cytology. Fourteen of the 16 patients (88%) had superior venacaval (SVC) obstruction. None of the patients with DHL without sclerosis displayed predominant mediastinal disease or SVC obstruction. In 15 of the 16 individuals, combination chemotherapy with Cyclophosphamide, Vincristine, Methotrexate with Leucovorin Rescue, and Cytosine Arabinoside (COMLA) was given with (11) or without (4) radiotherapy to the mediastinal mass. One individual received radiotherapy only. In four patients, chemotherapy with Bleomycin, Doxorubicin, Cyclophosphamide, Vincristine, and Prednisone (BACOP) was given following failure of the COMLA program. Of the 13 patients who have completed their primary therapy, only three are long-term survivors in complete remission. (no Refs)

39. SURGICAL RESECTION IN THE TREATMENT OF ABDOMINAL UNDIFFERENTIATED LYMPHOMAS, INCLUDING BURKITT'S (MEETING ABSTRACT)

Janus C, Sariban E, Alabaster O, Magrath IT
National Cancer Institute, Bethesda, MD, 20205
Proc Am Soc Clin Oncol; 1:C-622 1982

Although surgery is considered to play a minor role in the specific management of lymphoma, a study in African Burkett's lymphoma (BL) suggested that resection of greater than 90% of intraabdominal tumor greatly improves the patient's prognosis. Our results in 14 patients with abdominal ULs (BL and non-BL) confirm this. The age range was 3-35 (median 14). Twelve were males. Twelve had ileocecal tumor. Other sites were ovarian, renal and retroperitoneal/thigh tumoirs. Eight patients presented with an acute abdomen, and 5 had intestinal obstruction. No patient had evidence of noncontiguous extraabdominal tumor. Treatment consisted of 5 cycles of CTX (cyclophosphanide) 1200 mgm/m2, ADR (adriamycin) 40 mgm/m2, VCR (vincristine) 1.4 mgm/m2, and Prednisolone 40 mgm/m2, for five days and a 42 hour MTX (methotrexate) infusion (total dose 2.7 Gm/m(2)) with leukovorin rescue on day 10. The first cycle consisted of CTX, alone, on day 1, and the MTX infusion on day 10. No patient received radiation. One patient with residual tumor achieved a partial response. One patient relapsed with a single nodule of disease in a BM examination but achieved CR (complete remission) again after intensive chemotherapy. All other patients have remained in CR. Thirteen are alive and disease free 9 to 46 months after presentation. We conclude that patients with abdominal UL which can be at least 90% resected have an excellent prognosis after 6 cycles of chemotherapy. (no Refs)

MALIGNANT LYMPHOMA: CASE REPORTS

40. MYCOSIS FUNGOIDES PRESENTING AS AREAS OF HYPOPIGMENTATION: A REPORT OF THREE CASES.

Zackheim HS, Epstein EH, Grekin DA, McNutt NS
133 Arch St., Redwood City, CA, 94062
J Am Acad Dermatol; 6(3):340-345 1982

Foci of mycosis fungoides (MF) in dark-skined patients are usually hyperpigemented. In two black patients (a 22-yr-old woman and a 46-yr-old man) and a 75-yr-old Hispanic woman with patch-stage MF, most or all MF areas were hypopigmented. Total-body applications of nitrogen mustard (HN2: 10 mg/day x 4 wk) caused 70% tumor regression in the oldest patient. She developed an enlarged lymph node after 3 mo of observation and was lost to follow-up 2 mo later. Total-body applications of carmustine (BCNU: 400-675 mg over 16-27 days) caused complete tumor regression in both black patients. The woman showed evidence of recurrent MF after 39 mo. The man developed a localized recurrence after 14 mo, which disappeared after 5 wk of topical BCNU (0.05% in ethanol) applications; he remained in remission 8 mo later. In all patients, the regressing MF foci and the normal skin became hyperpigmented. This reaction was transient in the normal skin. The MF foci developed about the same degree of pigmentation as the normal skin and remained in this stage during remission. In the man (whose mother and niece had lymphomas), MF was identified in biopsies of an erythematous plaque (present for about 8 yr) and a hypopigmented macular area of skin. This patient had been diagnosed as having vitiligo 16 yr previously, and had responded partially to intermittent methoxsalen-UV therapy. He said that areas of hypopigmented, macular skin had been present when the diagnosis of vitiligo was made (without a skin biopsy). This suggested that the 'vitiligo' may have represented an early stage of MF, although the late appearance of erythematous plaques argued against this possibility. These patients' paradoxical hyperpigmentation reactions to HN2 or BCNU suggested that MF foci contain some unidentified factor(s) that interfere with the pigmenting actions of these agents. (7 Refs)

MALIGNANT LYMPHOMA: SELECTED REPORTS ON ETIOLOGY AND EPIDEMIOLOGY

41. MALIGNANT LYMPHOMA IN FIRST-DEGREE BLOOD RELATIVES.

Haim N, Cohen Y, Robinson E
Dept. Oncology, Rambam Medical Center, Haifa, Israel
Cancer; 49(10):2197-2200 1982

The statistical significance of familial lymphoma in first-degree blood relatives was evaluated for the series of all lymphoma cases referred to our department since 1968. Four pairs of immediate relatives with Hodgkin's disease (HD) were found among 183 patients diagnosed between 1960 and 1980. The expected number during that period was 0.45. Thus, close relatives of HD patients had about ninefold increased risk of the disease (p less than 0.005). Mixed-cellularity was the most common subtype in these familial cases (6/8 patients). There were three pairs of close relatives with non-Hodgkin's lymphoma (NHL) among 532 patients diagnosed during the same period, 1960-1980. The expected number was 3.86. These findings further indicate that HD may differ from NHL with regard to familial clustering. (Author abstract) (30 Refs)

42. MALIGNANT LYMPHOMA AMONG DRUG ADDICTS (MEETING ABSTRACT)

Cheung TW, Silber R
Department of Medicine, New York University School of Medicine, New York, NY, 10016
Proc Am Soc Clin Oncol; 1:C-13 1982

Lymphadenopathy is a frequent finding in parenteral drug addicts. The recent admission of several addicts to Bellevue Hospital in whom the diagnosis of malignant lymphoma was made prompted us to analyze the incidence of this disorder in an addict population. Age, sex and race-matched controls were selected from the hospital registry by admission date. Eighteen cases of malignant lymphoma were observed among parenteral drug addicts in Bellevue Hospital from 1970 to 1981. There were ten cases of Hodgkin's Disease and eight cases of non-Hodgkin's lymphoma. The most common presenting findings were lymphadenopathy and fever. In this respect drug addicts with lymphoma did not differ from the general population. Analysis by matched pair controls using the chi-square test showed that lymphoma was more likely to occur in drug addicts than among matched controls. When the incidence of acute leukemia in the same hospital addict population was determined, no increase was observed. The apparent increase in incidence of malignant lymphoma among addicts suggests that further studies of this association should be carried out. (1 Ref)

43. INCREASED FREQUENCY OF HLA-DR5 IN MYCOSIS FUNGOIDES AND KAPOSI'S SARCOMA (MEETING ABSTRACT)

Safai B, Pollack MS, Myskowski L, Dupont B
Sloan-Kettering Institute for Cancer Research, New York, NY, 10021
Fed Proc; 41(3):414 1982

Mycosis Fungoides (MF) is a cutaneous T-cell lymphoma while Kaposi's Sarcoma (KS) is a multicentric neoplasm which often has its primary manifestation in the skin. Although the exact mechanism for initiation of either disease is still unknown, a viral mechanism has been suggested in both cases. Specifically, retroviruses have been associated with some tumor cell lines of MF, and cytomegaloviruses have been associated with KS. In order to investigate the possible role of HLA-associated variations in genetic susceptibility, 64 patients with histologically documented MF and 32 patients with histologically documented KS were typed for HLA-A,B,C antigens. Most of these patients were also typed for HLA-DR antigens. A significant increase in DR5 was the only statistically significant deviation in HLA antigen frequencies in either group (50% in MF and 60% in KS in comparison with 20% in controls). The increase in DR5 was especially striking in the subgroup of KS patients with the particularly aggressive form of KS recently described in young homosexual males. HLA-DR5 has also been associated with scleroderma and juvenile rheumatoid arthritis. Immunologic alterations are involved in the pathogenesis of both, but viral infection may also be a factor. The associations of MF and KS with DR5 thus suggest that some individuals with the DR5 antigen may be at higher genetic risk for virally initiated neoplastic diseases, possibly through an HLA-linked effect in the immune system. (no Refs)

MALIGNANT LYMPHOMA: SELECTED PRE-CLINICAL STUDIES

44. INTRACEREBRAL ADOPTIVE IMMUNOTHERAPY OF A MURINE LYMPHOMA ANTIGENICALLY ALTERED BY DRUG TREATMENT IN VIVO.

Romani L, Fioretti MC, Bianchi R, Nardelli B, Bonmassar E
Inst. Pharmacology, Univ. Perugia, Via del Giochetto, Perugia 06100, Italy
JNCI; 68(5):817-822 1982

Intracerebral tumor neutralization assay and adoptive immunotherapy with in vitro sensitized lymphocytes were done in immunodepressed mice challenged intracerebrally with L5178Y/DTIC lymphoma, a tumor subline antigenically altered by treatment with 5-(3,3-dimethyl-1-triazenyl)-1H-imidazole-4-carboxamide (DTIC) in vivo. Primary cytotoxic T-lymphocytes (CTL) were generated in vitro against L5178Y/DTIC cells with the use of splenocytes of histocompatible (BALB/cCr x DBA/2Cr)F1 donors. The extent of antitumor activity of CTL was evaluated by the measurement of tumor cell proliferation in the brain, as judged by the 125I-labeled 2'-deoxyuridine uptake values and by survival times of recipient mice. The results of the experiments showed: (a) CTL were highly effective in inhibiting tumor growth when they were injected along with L5178Y/DTIC tumor cells in a Winn-type neutralization assay; (b) the tumor inhibition mediated by CTL was specific, since no antilymphoma effects were detected when CTL sensitized against L5178Y/DTIC line were admixed with the parental L5178Y tumor or with other unrelated lymphoma cells; and (c) local adoptive immunotherapy with CTL given on Day 1,3, or 5 after the intracerebral challenge with L5178Y/DTIC lymphoma substantially impaired tumor cell proliferation and significantly increased survival times of recipient leukemic mice. (Author abstract) (37 Refs)

45. GROWTH INHIBITION (GI) OF UNDIFFERENTIATED LYMPHOMA (UL) CELLS BY SURFACE IGM MODULATION (MEETING ABSTRACT)

Parsons RG, Magrath IT
National Cancer Institute, Frederick Cancer Research Facility, Frederick, MD, 21701
Proc Am Assoc Cancer Res; 23:1005 1982

We have initiated a series of studies to determine the effects of surface IgM modulation on the growth of human UL cell lines. IgM modulation was affected with low doses (7ug/ml) of anti-IgM (u specific). The majority (5/7) of the American UL cell lines showed major GI (53-94%) as a result of surface IgM modulation. GI (greater than 30%) was not detected in any African Burkitt's lymphoma cell lines (3), Epstein Barr Virus (EBV)-transformed cord blood lymphocyte lines (3), or other EBV-containing lymphoblastoid cell lines (2). American UL cell lines inhibited by anti-Igm treatment did not contain the EBV genome, whereas lines which displayed weak GI were EBV+. GI of the American UL cell lines was observed following treatment with antibodies directed against u-heavy chain or the specific light chain class (kappa) that each cell line displayed, however GI was not detected following exposure of the cells to F(ab)'2 fragments directed against IgM heavy chain or antisera against other cell surface determinants. GI occurred rapidly with detectable effects at 2-6 hours after exposure to antibodies and maximum inhibition of (3H)-thymidine incorporation at 24 to 48 hours after treatment. GI was not associated with marked cytotoxicity. We have previously hypothesized that the American UL cells represent immature B-lymphocytes. This GI effect may be related to the induction of tolerance in neonates by anti-IgM antisera. (no Refs)

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HODGKIN'S DISEASE: DIAGNOSIS AND STAGING

1. IMAGING TECHNIQUES FOR STAGING ABDOMINAL HODGKIN'S DISEASE.

Castellino RA
Div. Diagnostic Radiology, Stanford Univ. Sch. Medicine, Stanford, CA, 94305

Cancer Treat Rep; 66(4):697-700 1982

Choice of imaging techniques for staging abdominal Hodgkin's disease (HD) depends on the patterns of involvement; the

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sensitivity, specificity, and accuracy of the available studies; and the type of information needed. Sites frequently involved by tumor, including para-aortic, paracaval, parailiac, and splenic hilar lymph nodes, and the spleen, should be routinely evaluated. Specific sites, regardless of the incidence of disease at that site, should be studied if appropriate signs or symptoms are present. Imaging techniques specifically used for the retroperitoneal lymph nodes, other lymph node groups, the spleen, liver, and gastrointestinal and genitourinary tracts are described. Possible choices of techniques include plain film radiography such as conventional tomography and positive-contrast studies, angiography including lymphography, radionuclide studies, ultrasonography, and computerized tomography. An approach to imaging the abdomen and pelvis in newly diagnosed, previously untreated patients with HD for staging purposes is outlined. (8 Refs)

2. CT SCAN MODIFICATION IN THE TREATMENT OF MEDIASTINAL HODGKIN'S DISEASE.

Rostock RA, Giangreco A, Wharam MD, Lenhard R, Siegelman SS, Order SE
Dept. Radiation Oncology, Johns Hopkins Hosp., 600 North Wolfe St., Baltimore, MD, 21205
Cancer; 49(11):2267-2275 1982

Seventy-one patients with Hodgkin's disease who were initially treated at Johns Hopkins with radiation or radiation-chemotherapy from 1975-1980 had a 5-yr cumulative disease-free survival of I-A--100% (12 patients); II-A--85% (33 patients); II-B--83% (7 patients); III-A--75% (10 patients); and III-B--66% (9 patients). Fifty patients with mediastinal masses at the time of treatment demonstrated no marginal misses, two mediastinal recurrences (96% local control), and three lung disseminations. CT scan data yielded stage and treatment modification in 60% (9/15) of recent patients with mediastinal Hodgkin's disease. This demonstrates the need for routine thoracic scans and individual treatment planning in all mediastinal cases. Recommendations for combination treatment in early stage disease are made only for pericardial or extrathoracic chest wall extension based on CT scan findings, our low failure rates, radiation organ tolerances, and available relapse data in the literature, not arbitrary size designations from upright chest radiographs. It can be concluded that patients with mediastinal Hodgkin's disease require CT scan analysis to identify unusual patterns of presentations, sites at risk, and to allow for proper application of radiation portals and/or chemotherapeutic management. (Author abstract) (34 Refs)

3. CHROMOSOMES IN HODGKIN'S DISEASE.

Rowley JD
Box 420, 950 E. 59th St., Chicago, IL, 60637
Cancer Treat Rep; 66(4):639-643 1982

Chromosome studies in lymph nodes from patients with Hodgkin's disease have been limited by the low yield of dividing cells. Of 25 consecutive involved lymph nodes, 12 had no mitotic cells, 3 had only normal cells, 7 had a mixture of normal and abnormal cells, and 3 had only abnormal cells. Correlating histology with the karyotype, 66% of unsuccessful samples were of the nodular sclerosing type. The majority (58%) of samples with no dividing cells were from previously treated patients. Distinct clones were obtained in samples from only 4 of 10 patients with abnormal cells. Samples from the other six patients had single abnormal cells with bizarre marker chromosomes; these single cells probably represent the only dividing malignant cell. The high failure rate and the low number of clear-cut aneuploid clones in Hodgkin's disease contrast markedly with other lymphomas in which 80% of the samples yield mitotic cells that represent an aneuploid clone in virtually every instance. (Author abstract) (22 Refs)

4. HISTOCHEMISTRY OF HODGKIN'S DISEASE.

Beckstead JH, Warnke R, Bainton DF
Dept. Pathology, HSW 501, Univ. California Sch. Medicine, San Francisco, CA, 94143
Cancer Treat Rep; 66(4):609-613 1982

The histochemistry of Hodgkin's cells is controversial. Limited numbers and the variety of techniques used make comparisons difficult. Acid phosphatase and nonspecific esterase have been the two enzymes most frequently tested because the presence of these enzymes has been thought to be characteristic of histiocytes. Despite the controversial results, there studies have frequently figured prominently in arguments about the cell of origin in Hodgkin's disease. Authors identifying the presence of acid phosphatase and nonspecific esterase have generally favored a mononuclear phagocyte origin; those with negative results have favored a lymphoid origin. We have evaluated a series of 21 cases of Hodgkin's disease using tissues embedded in plastic and tested for acid phosphatase and nonspecific esterase. We found that Hodgkin's cells were frequently positive for acid phosphatase (20 of 21 cases) and/or nonspecific esterase (18 of 21). The reactions are weak and sensitive to inhibition by processing procedures. The reaction patterns are unusual for lymphoid cells and histiocytes. The finding is similar to that seen in interdigitating reticulum cells, a specialized cell found in the paracortex of human lymph nodes. (Author abstract) (25 Refs)

5. PROGNOSTIC FACTORS IN PATHOLOGIC STAGE III HODGKIN'S DISEASE.

Hoppe RT, Cox RS, Rosenberg SA, Kaplan HS
Div. Radiation Therapy, Dept. Radiology, Stanford Univ. Medical Center, Stanford, CA, 94305
Cancer Treat Rep; 66(4):743-749 1982

The results of treatment of pathologic Stage (PS) III Hodgkin's disease at Stanford University were examined during two treatment periods. Between 1968 and 1974, patients with PS IIIA or PS IIIB disease were treated with either total lymphoid irradiation (TLI) alone or followed by adjuvant combination chemotherapy (CHX). Between 1974 and 1980 all PS IIIB patients were treated with combined modality therapy, but PS IIIA patients continued to be treated with either TLI or TLI plus CHX. The adverse prognostic influence of systemic (B) symptoms was clearly evident among patients treated with TLI alone. However, with combined modality therapy, the outcome of therapy improved for both PS IIIA and PS IIIB patients, and systemic symptoms no longer had an adverse influence. The outcome of therapy for all patients with PS IIIA disease was analyzed in detail, comparing 102 patients treated with TLI alone with 99 patients treated with TLI plus CHX. An attemp was made to identify prognostic factors in PS IIIA disease. Clinical stage, age, sex, extranodal extension, number of sites involved, and 'anatomic substage' all failed to influence prognosis. The only important prognostic factor was the extent of splenic involvement. Patients with extensive splenic involvement had a significantly worse freedom from relapse rate than patients with minimal or no splenic involvement when treated with TLI alone. The adverse influence of extensive splenic disease was independent of the extent of subdiaphragmatic nodal involvement. The use of TLI plus CHX significantly improved freedom from relapse among patients with extensive splenic involvement; however, survival was improved to a lesser degree. These results support the use of combined modality therapy for PS IIIA patients with extensive splenic involvement. Other PS IIIA patients can be treated as effectively with TLI alone as with combined modality programs. (23 Refs)

6. MISTAKEN CLINICAL AND PATHOLOGIC DIAGNOSES OF HODGKIN'S DISEASE: A SOUTHWEST ONCOLOGY GROUP STUDY.

Miller TP, Byrne GE, Jones SE
4-West Clinic Facility, Arizona Health Sciences Center, 1501 N. Campbell Ave., Tucson, AZ, 85724
Cancer Treat Rep; 66(4):645-651 1982

Expert hematopathology review of initial diagnostic material was required for patients registered in a Southwest Oncology Group trial of advanced Hodgkin's disease (HD). Of 287 cases reviewed, 36 (13%) had been misdiagnosed as HD. The clinical and histologic features of the first 180 patients reviewed by the expert panel, including 21 (12%) patients for whom errors in diagnosis were discovered, were retrospectively analyzed to ascertain why mistakes in diagnosis had occurred. The most common error in pathologic interpretation was to confuse other malignant lymphomas with HD (14/21 patients), particularly large cell lymphomas with pleomorphic features and Reed-Sternberg-like cells. Rare conditions (Lennert's lymphoma or angioimmunoblastic lymphadenopathy) were also confused with HD. Mixed-cellularity and lymphocyte-depleted HD were the most frequently mistaken cell types (14/21 patients) and nodular-sclerosing HD was the least frequently mistaken (2 of 21). The clinical features of these 21 patients showed a high incidence of unusual extranodal sites of disease involvement including thyroid (1 patient), ovary (1), skin (2), bone (3), and lung (7). We next analyzed the clinical features of the remaining 107 cases in order to prospectively identify, based on atypical clinical presentations, patients who might not have HD. Subsequent histologic review revealed mistaken diagnosis in 15 patients (14%). Eight of the 15 patients (53%) were correctly identified as having disease other than HD on the basis of clinical presentation alone. Atypical clinical presentations, particularly unusual extranodal sites of disease along with a presumptive diagnosis of mixed cellularity or lymphocyte-depleted HD, should forewarn the clinician and the pathologist of a possible error in diagnosis. (Author abstract) (8 Refs)

7. CHANGING PATTERNS OF HODGKIN'S DISEASE AT AUTOPSY: A 25-YEAR EXPERIENCE AT THE NATIONAL CANCER INSTITUTE, 1953-1978.

Grogan TM, Berard CW, Steinhorn SC, Hankey BF, Kant JA, Miliauskas JR, Young RC, DeVita VT
Dept. Pathology, Coll. Medicine, Health Sciences Center, Univ. Arizona, Tucson, AZ, 85724
Cancer Treat Rep; 66(4):653-665 1982

The pathologic findings at autopsy in 124 patients with an initial diagnosis of Hodgkin's disease (HD) were evaluated to assess the effects of treatment on the anatomic extent and histologic appearance of residual HD. Further, the effects of duration of disease, vascular invasion, and histologic subtype at diagnosis on sites of involvement were considered. The 124 autopsied cases came from a cohort of 345 patients admitted for treatment at the National Cancer Institute between 1953 and 1969, with followup extended to 1978. The pathologic review included extensive organ sampling; greater than 12,000 slides were reviewed. The study period spans 25 yr, ranging from a period of palliative therapy (81 cases, pre-1965) to the modern curative treatment era (43 cases, 1965 or later). A distinct reduction in the extent of disease at autopsy was noted in the group treated with curative intent. Reduced involvement was the rule for most, but not all, organ sites, with the reduction greater for certain histologic types. Some organs had a comparable incidence of involvement with early and late deaths. Histologic assessment identified an atypical monomorphic form of residual HD (treatment-altered HD) in patients from both treatment eras but most consistently in the post-1965 group. Vascular invasion occurred in 43% of cases. The incidence of extranodal involvement was considerably higher in patients with vascular invasion, indicating that vascular spread is a factor in extranodal spread and in lethal cases of HD. (Author abstract) (14 Refs)

8. ANATOMIC SUBSTAGES OF STAGE IIIA HODGKIN'S DISEASE: FOLLOWUP OF A COLLABORATIVE STUDY.

Stein RS, Golomb HM, Wiernik PH, Mauch P, Hellman S, Ultmann JE, Rosenthal DS, Flexner JM
A-3311 Vanderbilt Hosp., Nashville, TN, 37232
Cancer Treat Rep; 66(4):733-741 1982

The clinical significance of anatomic substage was reassessed in a previously reported series of 130 patients with Hodgkin's disease in pathologic Stage IIIA. For 100 patients, followup was greater than 8 years. By definition, Stage III1 disease includes involvement of spleen or splenic, celiac, or portal nodes, or any combination of these; Stage III2 disease includes involvement of para-aortic, iliac, or mesenteric nodes, with or without upper abdominal involvement. Both 8-year relapse-free survival (71% versus 40%) and 8-year overall survival (80% versus 54%) were better in Stage III1A than in III2A patients (p less than 0.001). For Stage III1A, relapse-free survival was better in patients receiving radiotherapy and chemotherapy than in patients receiving radiotherapy alone as initial treatment (92% versus 60%, p less than 0.002). However, 8-year overall survival rates in these two treatment groups were not significantly different (88% versus 76%, $p = 0.20$). For Stage III2A, both relapse-free survival at 8 years (84% versus 19%, p less than 0.001) and overall survival at 8 years (84% versus 41%, p less than 0.01) were superior in patients receiving combined modality therapy. Anatomic substage is a critical prognostic variable, especially if standard total nodal radiotherapy is considered as one of the therapeutic options. (Author abstract) (10 Refs)

9. THE STRATEGIC ROLE OF LAPAROTOMY IN STAGING HODGKIN'S DISEASE.

Larson RA, Ultmann JE
(c/o Ultmann), Univ. Chicago Cancer Res. Center, Box 444, 950 East 59th St., Chicago, IL, 60637
Cancer Treat Rep; 66(4):767-774 1982

The value of laparotomy in staging patients with Hodgkin's disease (HD) is reviewed. Staging requires surgical biopsy, detailed history, complete physical examination, laboratory studies, radiologic studies, and bone marrow biopsy. Under certain conditions, whole-chest tomography, computed tomography of the thorax, iv pyelography, ultrasound, inferior vena cavagram, skeletal radiographic survey, liver biopsy, laparoscopy, and exploratory laparotomy with splenectomy may be necessary; the latter if management decisions depend on identification of abdominal disease. Useful ancillary procedures include whole-body 67Ga scanning, liver and spleen scans, bone scan and an estimate of the patient's delayed hypersensitivity. When treatment strategy is based on clinical staging alone, some patients will be over-treated and some under-treated. Pathologic staging provides greater homogeneity of case material and a truer description of prognostic factors when comparing data on HD from different institutions. Current controversies regarding HD staging are discussed. Contradictory conclusions from different studies may be explained in part by the significant differences in both staging and treatment protocols. There may be only two stages of HD in terms of therapy and curability: nodal disease of limited extent which is curable with irradiation of involved lymph nodes alone, and disseminated disease which requires systemic therapy. A strategy for treating HD patients based on clinical staging alone is presented. Pathologic staging allows individualization of treatment. Second-look laparotomies do not appear to be cost effective; current followup consists of observation for relapse. Salvage therapy varies depending on the pattern of relapse. (23 Refs)

10. POSTTREATMENT LAPAROTOMY AS A GUIDE TO MANAGEMENT IN PATIENTS WITH HODGKIN'S DISEASE.

Sutcliffe SB, Wrigley PF, Timothy AR, Dorreen MA, Shand WS, Stansfeld AG, Jones AE, Malpas JS, Lister TA
Dept. Radiation Oncology, Princess Margaret Hosp., 500 Sherbourne St., Toronto, Ontario, M4X 1K9, Canada
Cancer Treat Rep; 66(4):759-765 1982

Staging laparotomy and splenectomy were performed on 46 adult patients after combination chemotherapy for advanced Hodgkin's disease (HD). There was no preoperative evidence of intra-abdominal disease in 32 patients, 27 of whom were in complete clinical remission, while 5 had only residual mediastinal abnormalities. In the remaining 14 patients, there was clinical suspicion of active HD. Histologically abnormal HD was detected in 19 of the 46 (41%) operations. Active abdominal HD was detected in 6 of 46 patients (13%) or in 6 of 19 patients having previous evidence of intra-abdominal disease (31%). The spleen was involved in all patients, and in two of these patients there was evidence of both active and ablated disease. Pathologic evidence of ablated HD was detected in 13 patients. The prediction of active intra-abdominal HD, by lymphography or by computerized tomographic scanning, following mustine, vinblastine, procarbazine, and prednisolone therapy, was frequently inaccurate. There was no operative mortality. Morbidity was similar to that of pretreatment laparotomy. At a median follow up of 26.5 months (range, 5-59), 39 of 40 patients with no evidence of active abdominal HD remain in continuous remission. The contribution of posttreatment laparotomy toward the management of patients with HD is discussed. (Author abstract) (15 Refs)

11. SURGICAL RESTAGING OF HODGKIN'S DISEASE.

Goodman GE, Jones SE, Villar HV, Silverstein ME, Dabich L, Newcome SR, Southwest Oncology Group
(c/o Jones) Dept. Internal Medicine, Univ. Arizona Health Sciences Center, 4-West Clinic Facility, Tucson, AZ, 85724
Cancer Treat Rep; 66(4):751-757 1982

Twenty-six patients with Hodgkin's disease were restaged both clinically and surgically within 2 months of completing their planned chemotherapy. Six patients (23%) had surgically proven persisting disease. Patients were divided into three groups: Group I -8 patients had normal findings at clinical restaging and all were free of disease at surgery; Group 2-13 patients had abnormal findings at clinical restaging, but only 2 (15%) were surgically documented to have persistent disease; and Group 3-5 patients had incomplete clinical restaging but, because of initial bulky disease, underwent surgical restaging, which showed that four patients had residual disease. The spleen was the site of persistent disease in all six patients with residual disease; four also had para-aortic nodal involvement. All 20 patients in pathologically documented complete remission remain relapse-free, with a mean follow of 26 months. This is significantly better (p less than 0.001) than the 21% relapse rate for 224 comparable patients in complete remission established by clinical but not surgical restaging. It appears that surgical restaging provides useful prognostic and therapeutic information in selected patients with Hodgkin's disease. (Author abstract) (14 Refs)

12. PROGNOSTIC SIGNIFICANCE OF MEDIASTINAL MASS IN CHILDHOOD HODGKIN'S DISEASE.

Roskos RR, Evans RC, Gilchrist GS, Burgert EO, Ilstrup DM
(c/o Gilchrist), Mayo Clinic and Mayo Foundation, Rochester, MN, 55901
Cancer Treat Rep; 66(4):961-968 1982

The records of 60 consecutive surgically staged children with newly diagnosed Hodgkin's disease were reviewed to determine the prognostic significance of the presence of a mediastinal mass. Mediastinal mass was present in 38 patients and was more common in (a) females, (b) children greater than 12 yr old, (c) association with nodular sclerosis or lymphocyte depletion histology, (d) those with 'B' symptoms, and (e) the presence of advanced disease stage. The presence of a mediastinal mass was associated with reduced disease-free survival, the effect being more significant with a mediastinum/thoracic ratio greater than 0.33. The presence of a mass, large or small, did not influence overall survival. (Author abstract) (18 Refs)

HODGKIN'S DISEASE: CLINICAL IMMUNOLOGY AND IMMUNOTHERAPY

13. IMMUNOHISTOCHEMICAL ANALYSIS OF THE DISTRIBUTION OF LYMPHOCYTE SUBPOPULATIONS IN HODGKIN'S DISEASE.

Borowitz MJ, Croker BP, Metzgar RS
Dept. Pathology, Duke Univ. Medical Center, Box 3712, Durham, NC, 27710
Cancer Treat Rep; 66(4):667-674 1982

We studied the histologic distribution of lymphocyte subpopulations in Hodgkin's disease. Involved tissues from 15 patients were stained by an indirect immunoperoxidase procedure for a variety of lymphocyte surface antigens using monoclonal antibodies. In most cases, there were more T cells than B cells, and Reed-Sternberg cells were found in T-cell-rich areas. Except in lymphocyte-depleted Hodgkin's disease, helper-T antigen-positive (TH) cells greatly outnumbered cytotoxic-suppressor antigen-positive cells. Moreover, TH cells showed a preferential association with Reed-Sternberg cells. Lymphocytes surrounding Reed-Sternberg cells often expressed the transferrin receptor, a marker of cell activation. Our results do not support the hypothesis that the lymphocytes in Hodgkin's disease represent a cytotoxic T-cell response to neoplastic cells, except perhaps in the lymphocyte-depleted subtype. (Author abstract) (24 Refs)

14. DISTINGUISHING FEATURES OF THE IMMUNOLOGY OF HODGKIN'S DISEASE IN CHILDREN.

Tan CT, De Sousa M, Good RA
Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Cancer Treat Rep; 66(4):969-975 1982

Laboratory tests of immunologic function were done in 96 children with Hodgkin's disease, at diagnosis and during and after treatment. Over the same period of time, 29 age-matched control children were tested. The results presented in this report indicate that the immunology of childhood Hodgkin's disease has some features that distinguish it from the immunologic features of the disease in adults: (a) no progressive lymphopenia was found with advanced clinical stages; (b) peripheral blood T-lymphocyte counts were normal or high, and slight B lymphocytopenias were observed in children at all stages of the disease; (c) in spite of normal T-lymphocyte counts, a defective response to phytohemagglutinin stimulation was seen at diagnosis; and (d) recovery of the phytohemagglutinin response occurred with treatment and was related to modality of therapy and prognosis. (Author abstract) (18 Refs)

15. IMMUNE STATUS OF UNTREATED PATIENTS WITH HODGKIN'S DISEASE AND PROGNOSIS.

Bjorkholm M, Wedelin C, Holm G, Ogenstad S, Johansson B, Mellstedt H
Dept. Medicine, Div. Hematology, Danderyd Hosp., S-182 88 Danderyd, Sweden
Cancer Treat Rep; 66(4):701-709 1982

In this study of 127 previously untreated adult patients with Hodgkin's disease and 167 age- and sex-matched controls, highly purified blood lymphocytes were studied for E+ receptors; their spontaneous DNA synthesis and that induced by concanavalin A, pokeweed mitogen, or purified protein derivative of tuberculin were measured as incorporation of 14C-thymidine. T-cell counts and the response to mitogens and antigen were significantly decreased in the patients, while the spontaneous lymphocyte activity was increased. Forty-nine patients had died after a mean observation time of 6 yr. In these patients, there had been an increase in spontaneous DNA synthesis and a decrease in that induced by mitogens and antigen. These differences also remained significant when patients who died were compared with surviving patients in Stages I-II. The 5-yr survival rate of 'bad immunology' patients was 30% as compared to 80% for the remainder. We suggest that these lymphocyte tests should be considered in an 'immunologic staging system,' which may give guidance in the future management of patients with Hodgkin's disease. (Author abstract) (25 Refs)

16. EFFECT OF THE METHANOL EXTRACTION RESIDUE OF BACILLUS CALMETTE-GUERIN IN ADVANCED HODGKIN'S DISEASE.

Cooper MR, Pajak TF, Nissen NI, Brunner K, Stutzman L, Bank A, Falkson G, Barker BE, Haurani FI, Richards F, Gottlieb A, Holland JF
Dept. Medicine, Section Hematology/Oncology, Bowman Gray Sch. Medicine, Winston-Salem, NC, 27103
Cancer; 49(11):2226-2230 1982

One-hundred-ninety-six patients with Stage III and IV Hodgkin's disease were prospectively randomized to receive either treatment with the methanol extraction residue of Bacillus Calmette-Guerin (MER/BCG) or no immunotherapy. Prior to the MER/BCG randomization, patients received six courses of induction and 2 yr of maintenance chemotherapy so that a group with a presumptively low tumor burden could be established. Only patients achieving a complete remission were evaluated. During the first 2 yr of immunotherapy, the MER/BCG group had a relapse frequency twice that of controls. The overall crude relapse frequency and disease-free survival were similar between the two treatment groups. The MER/BCG dose schedule used in this study was associated with a high frequency of unacceptable toxicity. Ulcerations of greater than 1 cm occurred in one-third of the patients with associated pain, fever, and occasional lymphadenopathy. A high degree of patient noncompliance (36%) was observed. Age ($p = 0.002$), prior radiotherapy ($p = 0.032$), and chemotherapy ($p = 0.044$) were prognostic factors found to significantly influence remission duration. These factors were balanced between patients treated with immunotherapy and those who were not. MER/BCG therapy did not significantly delay or prevent relapse. (Author abstract) (32 Refs)

HODGKIN'S DISEASE: CHEMOTHERAPY

17. CYCLIC DELIVERY OF MOPP AND ABVD COMBINATIONS IN STAGE IV HODGKIN'S DISEASE: RATIONALE, BACKGROUND STUDIES, AND RECENT RESULTS.

Bonadonna G, Santoro A, Bonfante V, Valagussa P
Istituto Nazionale Tumori, Via Venezian, 1, 20133 Milan, Italy
Cancer Treat Rep; 66(4):881-887 1982

This paper summarizes the experience of the Cancer Institute of Milan with doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD) chemotherapy in various stages of Hodgkin's disease, with special emphasis on the cyclic delivery of mechlorethamine, vincristine, prednisone, and procarbazine (MOPP) and ABVD in the primary treatment of Stage IV disease. Six cycles of ABVD yielded a complete remission (CR) rate similar to that of MOPP. ABVD combined with radiotherapy in 153 patients with Stage IIB, IIIA, or IIIB disease was superior to MOPP plus radiotherapy in the CR induction, particularly in the presence of nodular sclerosis histology and B symptoms, as well as in the relapse-free survival of patients with pathologic Stage IIIA disease. Total survival was similar between the two treatment groups, but, compared to MOPP, ABVD chemotherapy was associated with a lower incidence of delayed toxic effects such as azoospermia, prolonged amenorrhea, and cancerigenesis. ABVD induced CR in 59% of 54 patients resistant to MOPP. The cyclic delivery of MOPP and ABVD was significantly superior to that of MOPP alone in terms of CR, freedom from disease progression, and relapse-free survival at 5 yr. Toxic effects were similar between the two treatment groups, but there was a higher incidence of vomiting and alopecia following ABVD chemotherapy; in the group given MOPP alone, one patient who had previously failed extensive irradiation developed acute nonlymphocytic leukemia. ABVD is confirmed to be an effective regimen that is non-cross-resistant to MOPP and devoid of late morbidity. Therefore, its administration, when alternated monthly with MOPP, offers the possibility to improve the cure rate of Hodgkin's disease. (18 Refs)

18. LONG-TERM COMPLICATIONS OF MOPP CHEMOTHERAPY IN PATIENTS WITH HODGKIN'S DISEASE.

Cunningham J, Mauch P, Rosenthal DS, Canellos GP
(c/o Mauch), Joint Center for Radiation Therapy, 50 Binney St., Boston, MA, 02115
Cancer Treat Rep; 66(4):1015-1022 1982

Two hundred and sixty-three patients in long-term remission from Hodgkin's disease were evaluated for complications of chemotherapy. All patients were interviewed by telephone conversation and reported complications were documented by chart review. Treatment consisted of mantle and para-aortic irradiation in 127 patients, total nodal irradiation (TNI) in 32, TNI and MOPP in 34, and mechlorethamine, vincristine, prednisone, and procarbazine (MOPP) chemotherapy alone or with lesser irradiation in 70. In this study, greater than 90% of the men who received MOPP remain infertile. In contrast, a substantial portion of female patients treated with MOPP chemotherapy have retained normal menses (58%) and only a small proportion had been persistent amenorrhea (9%). Five of eight female patients desiring families after MOPP chemotherapy have had normal children. The risk of developing a major infection requiring hospitalization was greatest in those patients who had received TNI and MOPP chemotherapy. The risk of developing a herpes zoster infection was greatest during or within the 1st yr following therapy and was greatest in those patients receiving combined radiation therapy and chemotherapy. Nearly 100% of patients continue to lead normal lives following treatment for Hodgkin's disease. Only a small percent of patients (1.5%) have been totally disabled following treatment. (Author abstract) (26 Refs)

19. EFFECT OF AGE ON THERAPEUTIC RESPONSE AND SURVIVAL IN ADVANCED HODGKIN'S DISEASE.

Peterson BA, Pajak TF, Cooper MR, Nissen NI, Glidewell OJ, Holland JF, Bloomfield CD, Gottlieb AJ
Univ. Hosp., Univ. Minnesota, Box 348, Mayo Building, 420 Delaware St. SE, Minneapolis, MN, 55455
Cancer Treat Rep; 66(4):889-898 1982

Although age is a recognized prognostic factor in advanced Hodgkin's disease, there are few data concerning the use of combination chemotherapy in patients greater than 60 yr. In two Phase III trials of the Cancer and Leukemia Group B, 385 previously untreated patients with Stage III or IV Hodgkin's disease received multidrug chemotherapy. All patients received a combination of either mechlorethamine or a nitrosourea, as well as a vinca alkaloid, procarbazine, and prednisone. Two hundred and five patients were less than 40 yr of age, 107 were 40-59 yr, and 73 were greater than or equal to 60 yr. The overall response rates in these three age groups were 70%, 66%, and 40%, respectively. Age at the time of diagnosis was the predominant factor affecting response, and the response rate was not significantly higher in those older patients who received full doses of chemotherapy. Age was also associated with an increased frequency of serious leukopenia and thrombocytopenia. The group of patients greater than or equal to 60 yr of age experienced the shortest median time to recurrence, 33 mo. The intermediate age group also had a shorter time to recurrence (median, 44 mo) than patients less than 40 yr (median not yet reached). The low complete response rate and the short duration of response in the patients greater than or equal to 60 yr of age resulted in a median survival time of 18 mo. Even when the analysis is restricted to just the older patients who received greater than or equal to 90% of the projected drug doses, the complete remission rate, the median time to recurrence (20 mo), and the duration of survival (27 mo) are still much shorter than in younger patients. (Author abstract) (29 Refs)

20. CHEMOTHERAPY FOR ADVANCED HODGKIN'S DISEASE' CONCLUSIONS FROM THE SOUTHEASTERN CANCER STUDY GROUP.

Gams RA, Durant JR, Bartolucci AA
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Cancer Treat Rep; 66(4):899-905 1982

The Southeastern Cancer Study Group has explored a variety of approaches to the management of advanced Hodgkin's disease. These have largely involved the use of nitrosoureas, especially BCNU (carmustine), alone or in combination with other agents. Initial Phase II trials of BCNU as a single agent in patients refractory to mechlorethamine demonstrated considerable antitumor activity. Exploratory experiments with BCNU in combination with alkylating agents, vinca alkaloids, and corticosteroids resulted in the development of the combination BVCPP (BCNU, vinblastine, cyclophosphamide, procarbazine, and prednisone). BVCPP, given only once monthly, produces at least a 65% complete response rate with minimal to moderate toxicity, making it an effective alternative to other regimens such as MOPP. Alternating BVCPP with a non-cross-resistant combination (doxorubicin, DTIC [dacarbazine], and bleomycin) offered no advantage in response rate or survival. Continued research with new agents and/or combined modality approaches is necessary in view of continued primary and secondary treatment failure with all regimens used for the management of advanced Hodgkin's disease. (Author abstract) (10 Refs)

HODGKIN'S DISEASE: RADIOTHERAPY

21. RESULTS OF LUNG IRRADIATION FOR HODGKIN'S DISEASE PATIENTS WITH LARGE MEDIASTINAL MASSES AND/OR HILAR DISEASE.

Lee CK, Bloomfield CD, Levitt SH
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Cancer Treat Rep; 66(4):819-825 1982

From 1970 to 1979, 130 patients with Hodgkin's disease were seen at the University of Minnesota and were treated with curative radiotherapy following surgical staging. Thirty-nine of the 130 patients had large mediastinal masses. Twenty patients with large mediastinal masses treated before 1975 received regular mantle-field irradiation. Our treatment technique was modified in 1975 because of frequent recurrences in the intrathoracic region in these patients. Between 1975 and 1979, patients with large mediastinal masses were treated with low-dose lung irradiation as an initial part of the mantle-field treatment. Nineteen patients were treated in this manner, and 16 of these 19 have been followed for greater than 24 months. Only one of the 16 patients has had a recurrence in the lung. We have not seen any serious acute or subacute pulmonary or cardiac complications after low-dose lung irradiation. The followup period is still too brief for the study of late complications. Analysis of our results with lung irradiation reveals excellent control of large mediastinal masses and significantly improved recurrence-free survival. (Author abstract) (26 Refs)

22. PATTERNS OF CARE OUTCOME STUDIES IN HODGKIN'S DISEASE: RESULTS OF THE NATIONAL PRACTICE AND IMPLICATIONS FOR MANAGEMENT.

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Cancer Treat Rep; 66(4):805-808 1982

In a statistically valid random sample of 387 patients selected from the national practice and treated with radiation therapy in 1973 for Hodgkin's disease, the 4-yr recurrence-free survival was: Stage IA, 82%; Stage IIA, 75%; Stage IIIA, 60%; and combined Stages IB-IIIB, 50%. Observations of in-field recurrence in 996 separate lymph node areas show no dose-response relationship between 3,000 and 5,000 rad. The use of chemotherapy in Stage IIIA Hodgkin's disease in the national practice is associated with a significant improvement in recurrence-free survival ($p = 0.01$). A group of 51 patients with Stages IA-IIIA Hodgkin's disease, ages 5-15, treated with radiation therapy alone, has a 92% recurrence-free rate at 3 yr with no major complications. (Author abstract) (18 Refs)

23. PROGNOSTIC PARAMETERS IN EARLY STAGE HODGKIN'S DISEASE.

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Int J Radiat Oncol Biol Phys; 8(5):837-841 1982

Results of initial treatment with radiation therapy alone observed in laparotomy-staged 101 patients (53 males, 48 females, 97 whites, 4 blacks) with Hodgkin's disease are described. The minimum follow-up period calculated from the first day of treatment was 36 mo, the max 112 mo, and av 64 mo. Eighty percent of the patients were followed 46 mo or longer. Of the 101 patients, 99 achieved complete response (CR) after irradiation treatment. The two patients who did not achieve CR were Stage II-B and Stage II-B. Twenty-eight patients have relapsed (28%) during the follow-up period. Eighty-two percent (23/28) of relapses occurred by 48 mo. The relapse for patients greater than 40 yr old was 38%, for those less than 40 yr old 27%. Fifty-four percent of those greater than 40 yr old survived 5 yr, and 87% of those less than 40 yr old. The incidence of relapse was slightly higher for patients with mixed cellularity histology as compared with those with nodular sclerosis. Patients with Stage I and II disease had a relapse rate of 23% (19/82) compared with 53% (9/17) for Stage III, but the actuarial survival at 5 yr was better for Stage III. Intrathoracic involvement was present in 53 patients of whom 22 relapsed (42%). In the 46 patients without the thoracic involvement the relapse rate was 13%. Patients with small mediastinal masses had a relapse rate of 28% compared with 45% for those with a large mass. Patients with systemic symptoms had a higher relapse rate than those without, but similar 5-yr survival. Nineteen patients received multi-agent chemotherapy at the time of relapse. Seven of these died with disease, three were alive with disease, and nine were free of disease. The overall salvage rate was 54% (15/28). (26 Refs)

24. COLLABORATIVE CLINICAL TRIAL FOR STAGE I AND II HODGKIN'S DISEASE: SIGNIFICANCE OF MEDIASTINAL AND NONMEDIASTINAL DISEASE IN LAPAROTOMY- AND NON-LAPAROTOMY-STAGED PATIENTS.

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Cancer Treat Rep; 66(4):775-787 1982

In this study, 460 eligible patients with Stage I and II Hodgkin's disease were randomized to treatment with involved field (IF) and extended field (EF) radiotherapy. Lymphangiogram was a requisite of the study. One hundred and seventy-seven patients were staged by laparotomy. The value of EF radiotherapy in improving survival over a 10-year follow up was studied. This effect was considered separately for patients staged by laparotomy, for patients staged by lymphangiogram alone, and for patients with and without initial mediastinal involvement. A substantial benefit was seen for the subgroup staged by lymphangiogram alone and without mediastinal disease, with 10-year survival rates of 80% for EF and 56% for IF. For all other groups staged by laparotomy or having mediastinal presentations 10-year survival rates were essentially the same, differing by less than 10 percentage points for IF and EF regimens. The advantage of EF treatment in lymphangiogram-staged nonmediastinal disease was realized only when the extended fields included the abdominal para-aortic area. (Author abstract) (14 Refs)

25. ROLE OF RADIATION THERAPY IN THE TREATMENT OF HODGKIN'S DISEASE.

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Cancer Treat Rep; 66(4):915-923 1982

We reviewed the results of 10 yr of experience in treating 405 patients with Stage IA-IIIB Hodgkin's disease at the Joint Center for Radiation Therapy. It appears that 'total nodal irradiation' may largely be avoided. For supradiaphragmatic Stage I and IIA disease, mantle and para-aortic irradiation result in excellent relapse-free survival except in patients with large mediastinal masses. Stage IIB patients can be treated similarly to those in Stage IIA. Stage IIIA patients treated with total nodal irradiation alone fare less well. Combined modality treatment improves survival markedly but may cause excessive complications. For Stage III1A, we currently recommend that patients be treated with mantle and para-aortic nodal irradiation, with chemotherapy used only in those who fail. We treat Stage III2A and IIIB patients with both chemotherapy and radiation. (Author abstract) (25 Refs)

26. LONG-TERM CARDIOVASCULAR EVALUATION OF PATIENTS WITH HODGKIN'S DISEASE TREATED BY THORACIC MANTLE RADIATION THERAPY.

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Cancer Treat Rep; 66(4):1003-1013 1982

The long-term cardiac effects of anterior-weighted thoracic mantle field radiotherapy were assessed in 25 patients treated for Hodgkin's disease. These patients underwent an evaluation that included a careful history and physical examination, ECG, M-mode echocardiogram, exercise ECG-gated radionuclide ventriculography, and cardiac catheterization. In these 25 patients evaluated 37-144 mo (median, 96) after completion of thoracic mantle radiotherapy, 8 had constrictive pericarditis; 8 had occult constrictive pericarditis; 3 had an abnormal response to fluid challenge; 3 had suspected or proven occlusive coronary artery disease; and 1 each had a cardiomyopathy and diminished functional capacity on exercise testing. Only one patient appears to be normal after evaluation. The clinical spectrum of delayed-appearing radiation-induced cardiac disease in patients treated by anterior-weighted thoracic mantle fields and our suggestions for its treatment are discussed. (Author abstract) (17 Refs)

27. THYROID NODULES AFTER HIGH-DOSE EXTERNAL RADIOTHERAPY. FINE-NEEDLE ASPIRATION CYTOLOGY IN DIAGNOSIS AND MANAGEMENT.

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JAMA; 247(23):3217-3220 1982

From 1974 to 1980, we studied six patients, five treated for Hodgkin's disease and one for a hemangioma, in whom thyroid nodules developed after high-dose (2,500 to 4,000 rad) thyroid radiation. Fine-needle aspiration cytology of the thyroid in five cases showed moderate to severe cellular atypia in four (3 of whom had elevated serum thyrotropin levels) and mild atypia in one (who was overtly hypothyroid). In the four with marked atypia, surgical pathology disclosed Hashimoto's thyroiditis in one, diffuse hyperplasia and epithelial atypia in two, and a sclerosing papillary carcinoma in one. Among five patients who had total thyroidectomy, three had carcinoma (microscopic papillary, papillary- follicular, or sclerosing papillary) in addition to one or more follicular adenomas or colloid nodules. Thyroid nodules and neoplasia may be more common than previously appreciated in patients exposed to high-dose radiation. (Author abstract) (20 Refs)

HODGKIN'S DISEASE: MULTIMODAL THERAPY

28. CHEMOTHERAPY AND COMBINED MODALITY THERAPY FOR HODGKIN'S DISEASE: A PROGRESS REPORT ON CANCER AND LEUKEMIA GROUP B STUDIES.

Bloomfield CD, Pajak TF, Glicksman AS, Gottlieb AJ, Coleman M, Nissen NI, Rafla S, Stutzman L, Vinciguerra V, Glidewell OJ, Holland JF
Box 277, Univ. Minnesota Hosp., Minneapolis, MN, 55455
Cancer Treat Rep; 56(4):835-846 1982

Between 1974 and 1977, the Cancer and Leukemia Group B (CALGB) initiated four studies which address current major questions in the therapy for Hodgkin's disease. The efficacy of chemotherapy alone as compared with combined modality therapy in patients with poor-prognosis Stages I and II is evaluated in CALGB 7751. Currently, both therapies produce very high complete remission rates in asymptomatic patients; the remission rate is better with combined modality therapy in symptomatic patients. Single and combined modality therapies are compared for Stage III patients in CALGB 7451. Complete remission rates have been similar, but relapse-free survival is superior for patients treated with total nodal radiotherapy followed by chemotherapy (p = 0.04). In particular, Stage IIIA patients with nodular sclerosis seem to benefit from the inclusion of radiotherapy in their initial treatment. In CALGB 7551, the efficacy of chemotherapy alone versus chemotherapy plus radiotherapy to areas of bulky disease is under study in patients with Stages IIIB and IV. Currently, a relapse rate of less than 10% has been seen among sites irradiated, and survival is best for patients treated with radiotherapy bracketed by chemotherapy. Finally, the role of two alternating non-cross-resistant combination chemotherapy programs is being studied in CALGB 7552. Relapse-free and overall survival is better with the doxorubicin-containing regimen than with either the alternating or alternate chemotherapy program. At present, the median followup for each of these studies is less than 5 years. Further observation is required to answere the critical question relating to prolonged disease-free survival and cure. (Author abstract) (23 Refs)

29. MULTIDISCIPLINARY TREATMENT OF ADVANCED HODGKIN'S DISEASE BY AN ALTERNATING CHEMOTHERAPEUTIC REGIMEN OF MOPP/ABDV AND LOW-DOSE RADIATION THERAPY RESTRICTED TO ORIGINALLY BULKY DISEASE.

Young CW, Straus DJ, Myers J, Passe S, Nisce LZ, Lee BJ, Koziner B, Arlin Z, Kempin S, Gee T, Clarkson BD
Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Cancer Treat Rep; 66(4):907-914 1982

Ninety-one evaluable patients with advanced Hodgkin's disease (patients with Stages IIB, IIIB, or IV disease and patients with stage IIIA disease who were greater than 35 yr old or had mixed cellularity or lymphocyte depletion histology) received chemotherapy with MOPP (mechlorethamine, vincristine, prednisone and procarbazine) and ABDV (doxorubicin, bleomycin, dacarbazine and vinblastine) given in alternating months; radiation therapy (RT) (2,000 rad in 2 wk) was given during Month 5 of therapy to the previously untreated patients through ports that were limited to the originally bulky disease. The complete remission rates observed were: 88% in previously untreated patients, 69% in patients who had had prior RT but minimal chemotherapy, and 50% in patients who had had prior heavy chemotherapy. The actuarial relapse-free survival rates at 4 yr, for patients who had complete remission, are: previously untreated, 84%; prior RT, 70%; and prior heavy chemotherapy, 30%. The total actuarial survival rates at 5 yr for all 118 patients, evaluable and nonevaluable, who were entered in the study, are: previously untreated, 80%; prior RT, 57%; and prior heavy chemotherapy, 40%. (Author abstract) (15 Refs)

30. INTERGROUP HODGKIN'S DISEASE IN CHILDREN STUDY OF STAGES I AND II: A PRELIMINARY REPORT.

Sullivan MP, Fuller LM, Chen T, Fisher R, Fryer C, Gehan E, Gilchrist GS, Hays D, Hanson W, Heller R, Higgins G, Jenkin D, Kung F, Sheehan W, Tefft M, Ternberg J, Wharam M
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Cancer Treat Rep; 66(4):937-947 1982

The intergroup study of involved-field (IF) radiotherapy, IF radiotherapy plus mechlorethamine, vincristine, prednisone and procarbazine (MOPP) chemotherapy, and extended-field (EF) radiotherapy for treatment of Hodgkin's disease in children has assessed 305 patients. Of these, 279 were 'not ineligible' (no immediate cause for disqualification). Among 223 randomized patients, 144 were evaluable, 131 had documentation of complete or partial remission, 20 of the remitters relapsed, and 2 died. Among 62 nonrandomized patients with favorable presentations (unilateral upper neck, unilateral inguinal, or massive mediastinal disease), 29 had documented remission, 2 relapsed, and none died. Length of initial disease control (LIDC) was used to measure duration of response. LIDC was best in patients given IF plus MOPP, and 95% are disease free. EF was better than IF radiotherapy ($p = 0.004$). Of the disease characteristics prognostic for response (stage, histologic subtype, and presence of symptoms), only the last factor had a statistically significant effect on LIDC ($p = 0.004$). Ninety-six percent of the patients survive. Using criteria developed by the committee, 23% of the staging procedures reviewed were nonevaluable and 28% of the radiotherapy treatments were nonevaluable. The necessity for criteria for evaluation of staging and treatment is certain. Length of follow-up is too short for correlations of treatment with significant late effects and for relevant therapeutic recommendations. (Author abstract) (10 Refs)

31. HODGKIN'S DISEASE IN CHILDREN: TREATMENT RESULTS WITH MOPP AND LOW-DOSE, EXTENDED-FIELD IRRADIATION.

Jenkin D, Chan H, Freedman M, Greenberg M, Gribbin M, McClure P, Saunders F, Sonley M
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Cancer Treat Rep; 66(4):949-959 1982

Combined therapy with mechlorethamide, vincristine, prednisone and procarbazine (MOPP) and extended-field irradiation for all children with Hodgkin's disease (except those with favorable clinical stage [CS] 1) was effective in disease control. Overall 5-yr survival and relapse-free survival rates were 92% and 82%, respectively. Only one of 27 CS 2 and 3 patients has relapsed (median follow-up, 4.3 yr). Two patients in complete remission died of viral infection. The cost-benefit ratio for such treatment remains to be determined. Morbidity was decreased by the omission of staging laparotomy with splenectomy and by reduction in radiation dose and to a lesser extent volume, but it was increased by the addition of MOPP. In such combined treatment, the smallest number of cycles of MOPP, the lowest radiation dose, and the smallest radiation volume that may be used without loss of treatment effectiveness remain to be determined. (Author abstract) (3 Refs)

32. HODGKIN'S DISEASE WITH DIRECT EXTENSION INTO PULMONARY PARENCHYMA FROM A MEDIASTINAL MASS: A PRESENTATION REQUIRING SPECIAL THERAPEUTIC CONSIDERATIONS.

Wiernik PH, Slawson RG
Baltimore Cancer Res. Center, Univ. Maryland Hosp., 22 S. Greene St., Baltimore, MD, 21201
Cancer Treat Rep; 66(4):711-716 1982

The significance of limited extranodal Hodgkin's disease involving pulmonary parenchyma by direct extension from a mediastinal mass (E stage) was evaluated in 177 patients with Stages IA-IIIB. Disease-free and total survival rates of four groups were compared: 58 patients without and 13 patients with pulmonary E stage treated with radiotherapy followed by six courses of MOPP (mechlorethamine, vincristine, procarbazine, and prednisone), and 86 patients without and 20 patients with E stage treated with radiotherapy alone. The 12-year- disease-free and total survival rates projected by life-table analysis were significantly poorer for E stage patients treated with radiotherapy alone. It is concluded that pulmonary E stage requires special therapeutic considerations if end results are to equal those obtained with standard radiotherapy for Hodgkin's disease confined to lymph nodes, and that combined modality therapy is one method by which pulmonary E stage may be treated successfully. (Author abstract) (21 Refs)

33. CONCLUSIONS FROM CLINICAL TRIALS OF THE SOUTHWEST ONCOLOGY GROUP.

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Section Hematology and Oncology, Dept. Internal Medicine, Univ. Arizona Health Sciences Center, 4-West Clinic Facility, Tucson, AZ, 85724
Cancer Treat Rep; 66(4):847-853 1982

Mature data from four clinical trials conducted by the Southwest Oncology Group from 1971 to 1978 for patients with all stages of Hodgkin's disease (HD) are reviewed in this paper. In the RAC 1 trial of Stage I and II HD we demonstrated that involved-field radiotherapy plus six courses of chlormethine, vincristine, procarbazine and prednisone (MOPP) chemotherapy improved relapse-free survival compared to standard radiotherapy alone ($p = 0.12$), especially in patients with B symptoms (p less than 0.03) or mediastinal disease ($p = 0.08$). However, at present, there is no significant difference in overall survival. In the CAR 1 study for patients with pathologic Stage IIB, IIIA, and IIIB HD, we demonstrated that three or four courses of MOPP before radiotherapy produced a 90% complete remission (CR) rate, with 70% of the patients remaining free of disease at 5 yr. In the CAR 2 study for patients with pathologic Stage IIIA or IIIB disease, we demonstrated that chemotherapy alone (MOPP-bleomycin) was as effective as combined modality treatment (MOPP-bleomycin plus radiotherapy) in terms of CR rate (85% versus 89%, respectively), relapse-free survival, and survival. For advanced stages of HD we added doxorubicin to our MOPP-bleomycin schedule and demonstrated that MOP-BAP produced a 77% CR rate compared to 67% for MOPP-bleomycin ($p = 0.10$). Moreover, MOP-BAP produced consistently superior CR rates and survival in patients with more prognostically favorable presentations of HD. Our new ongoing study (MOPP 6) incorporates many of the concepts derived from these earlier clinical investigations. (Author abstract) (24 Refs)

HODGKIN'S DISEASE: CASE REPORTS

34. FULMINANT INFECTION IN A SPLENECTOMIZED PATIENT WITH HODGKIN DISEASE. FATAL PNEUMOCOCCAL MENINGITIS IN A CURED PATIENT SEVEN YEARS AFTER SPLENECTOMY.

Corberand J, Marechal P, Geraud G, Schwarzenberg L
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Sem Hop Paris; 58(21):1325-1328 1982

Ten yr ago, because of the increasing number of patients recovering from Hodgkin disease, some authors advocated systematic laparotomy with splenectomy for more accurate staging in order to adjust therapy with more precision. This attitude now seems questionable because of the occurrence of several complications, particularly of life-threatening infections, which can be fatal even after recovery from Hodgkin disease. The case of a 23-yr-old male patient with Hodgkin disease Stage III A, histological Grade I, is reported. Chlorambucil, vincristine, procarbazine and prednisone (MOPP) chemotherapy, splenectomy and cobalt radiotherapy were followed by complete recovery. Seven yr later the patient died from fulminant pneumococcal meningitis. A review of the previously published cases show that prolonged prophylaxis with oral penicillin is mandatory in splenectomized patients. Immunization with the pneumococcal polysaccharide vaccine should be attempted even though the long-term results are still unknown. (Author abstract) (25 Refs) (In FRE)

HODGKIN'S DISEASE: SELECTED REPORTS ON ETIOLOGY AND EPIDEMIOLOGY

35. SOCIAL CLASS AND AGE AT DIAGNOSIS OF HODGKIN'S DISEASE: NEW EPIDEMIOLOGIC EVIDENCE FOR THE 'TWO-DISEASE HYPOTHESIS'.

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Cancer Treat Rep; 66(4):689-695 1982

The bimodality in the age-incidence pattern of Hodgkin's disease (HD) suggests that the disease may result from two causal pathways with differing age peaks. Among young adults, HD may develop as a rare consequence of a common infection (probably viral), with risk increasing with age at time of infection. However, among older persons, HD may result from other causes, probably similar to those of the other lymphomas. We evaluated this hypothesis in a population-based, case-control study in eastern Massachusetts involving 326 newly diagnosed cases (patients greater than or equal to 15 years of age) and 650 population controls. These subjects were compared for factors in childhood environment that influence age of exposure to common viruses, including subship size, parental education, and type of housing. Among young adult (15-39 years of age), risk of HD was associated with small family size, single-family housing, and relatively high maternal education, consistent with the delayed infectious exposure hypothesis. Among middle-aged persons (40-54 years of age), a similar pattern of social class risk factors was present. However, among older persons (greater than 55 years of age), risk was not associated with social class; if anything, patients were of somewhat lower social class background than controls. These findings are consistent with the 'two-disease hypothesis,' in that social class risk factors differed between younger and older persons. These findings, coupled with other epidemiologic observations, suggest that the pathogenesis of HD among older persons is independent of that among younger persons. (Author abstract) (10 Refs)

MALIGNANT LYMPHOMA: DIAGNOSIS AND STAGING

36. PROGNOSTIC SIGNIFICANCE OF THE LUKES AND COLLINS CLASSIFICATION IN PATIENTS TREATED WITH COMLA.

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Cancer Treat Rep; 66(5):1107-1111 1982

The Lukes and Collins classification was applied to 47 patients who received COMLA (cyclophosphamide, vincristine, methotrexate, leucovorin, and cytarabine) as initial treatment for diffuse histiocytic lymphoma (DHL). Pathologic staging was complete in 39 of 47 patients; 2 patients had Stage IIE disease, 17 had Stage III, and 28 had Stage IV. Complete remission, which was documented by extensive clinical restaging, was achieved in 25 (64%) of 39 patients with morphologic B-cell lymphomas and in only three of eight patients with non-B-cell lymphomas. The median duration of complete remission is significantly longer in patients with B-cell lymphomas than in those with non-B-cell lymphomas (45+ versus 13 mo, p less than 0.01). Among patients with DHL, median survival is significantly longer for those with B-cell lymphomas than for those with lymphoma of T-cell or indeterminate origin (60+ versus 6 mo, p less than 0.01). While DHL is regarded as a curable disease, patients not achieving complete remission are rarely salvaged; median survival for these patients was 10 mo. The Lukes and Collins classification allows us to identify patients with DHL in whom newer therapies are needed for initial treatment. Further study may enable us to identify additional unfavorable subsets in the B-cell category. (Author abstract) (12 Refs)

37. PRIMARY EXTRANODAL MALIGNANT NON-HODGKIN'S LYMPHOMAS (CLINICO-PATHOLOGIC CORRELATIONS IN 41 CASES).

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Haematologica (Pavia); 67(2):216-229 1982

A series of 41 consecutive, previously untreated patients (23 males, 18 females, 25-86 yr old, median age 57 yr) with primary extranodal non-Hodgkin's lymphoma was analyzed to verify the concept that tumors of extranodal or nodal origin have different natural histories. In 30 of the 41 patients, disease was limited to a solitary extranodal site (Stage IE); the other 11 patients had involvement of regional lymph nodes (Stage IIE). The most common sites of involvement were Waldeyer's ring (17 patients) and the gastrointestinal tract (10); other sites were skin (6), orbital tissue (3), lung (1), breast (1), thyroid (1), brain (1), and epidural tissue (1). Thirty-five patients (85%) achieved complete remission after initial treatment. Relapses were observed in 11 patients (31%) after disease-free intervals ranging from 13-50 mo. Two different patterns of relapse were observed: solitary relapse at the primary site and more disseminated recurrence. No solitary relapse in a second extranodal site was observed. The median survival for 37 evaluable patients with primary extranodal lymphomas was 51.4 mo. The median survival of the low-grade malignancy group exceeded 64 mo and was significantly better than that of the high-grade malignancy group (41.9 mo). Extent of initial disease significantly influenced survival. The median survival of patients with nodal lymphomas was 30.2 mo, while that of patients with extranodal lymphomas was 51.4 mo. Results indicated that patients with primary extranodal lymphomas often present with 'truly' localized disease that is potentially curable. (19 Refs)

38. CT OF RENAL AND PERIRENAL NON-HODGKIN LYMPHOMA.

Jafri SZ, Bree RL, Amendola MA, Glazer GM, Schwab RE, Francis IR, Borlaza G
Dept. Radiology, Univ. Michigan Medical Center, Box 13, Ann Arbor, MI, 48109
AJR; 138(6):1101-1105 1982

The CT findings from a retrospective review of 16 patients (32 kidneys) with non-Hodgkin lymphoma involving the kidney are presented. In all cases, computed tomography (CT) accurately depicted the presence, location, and size of the renal lesions and provided information about the adjacent retroperitoneum. CT was helpful in evaluating the course of the disease and its response to therapy. The CT manifestations of renal lymphoma included: solitary nodules (4 kidneys), multiple nodules (9), focal infiltration (5), diffuse infiltration (2), engulfment of the kidney by contiguous retroperitoneal disease (3), and renal enlargement (13 kidneys). Bilateral renal involvement was noted in seven patients. All 16 patients had retroperitoneal adenopathy. The CT findings of intraparenchymal renal nodules, renal infiltration, or renal engulfment by retroperitoneal disease in association with retroperitoneal adenopathy should suggest the possible diagnosis of renal lymphoma. (Author abstract) (22 Refs)

39. PRESENTATION OF MALIGNANT LYMPHOMA IN THE RECTUM.

Heule BV, Taylor CR, Terry R, Lukes RJ
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Cancer; 49(12):2602-2607 1982

Because of their rarity, rectal malignant lymphomas are generally included in the group of large intestine lymphomas. A study of eight cases of rectal lymphomas revealed distinctive clinicopathologic correlations. Using the Lukes-Collins classification of malignant lymphomas, the authors interpreted all the cases as B-cell lymphomas, supported by immunologic studies in four cases. Seven cases were classified diffuse follicular center cell (FCC) lymphomas; four as small cleaved FCC; and three as small noncleaved FCC. One case was interpreted as plasmacytoid lymphocytic lymphoma. Monoclonality was demonstrated by immunoperoxidase staining of cytoplasmic immunoglobulin in three cases and by immunologic surface marker studies in another case. The small noncleaved follicular center cell lymphomas presented as localized tumors (clinical Stage I), so-called primary lymphomas. The small cleaved follicular center cell lymphomas, by contrast, were part of a generalized lymphomatous process in three of the four cases with demonstrated involvement of the gastrointestinal tract elsewhere in two cases. (Author abstract) (17 Refs)

40. ULTRASTRUCTURE AND MORPHOMETRIC ANALYSIS OF HYPERTROPHIC NUCLEOLI IN NON-HODGKIN'S LYMPHOMA AND PHYTOHEMAGGLUTININ-STIMULATED LYMPHOCYTES.

Shapiro SH, Chang LY, Wessely Z, Klavins JV
Dept. Pathology, Queens Hosp. Center, 82-68 164th St., Jamaica, NY, 11432
Oncology; 39(4):234-241 1982

The ultrastructure of hypertrophic nucleoli in large cells from each of five successive cases of non-Hodgkin's lymphoma (regardless of predominant cell type) showed irregularly rounded or ovoid, mostly compact forms with few scattered light spaces. Occasional nucleolonemal forms were noted. Few ring forms or transitional forms between ring and compact or nucleolonemal types were present. Granular components occupied 78.5 +-1.0% of the mean total area of 132 lymphoma large cell nucleoli of all configurations studied. Hypertrophic nucleoli in 27 phytohemagglutinin (PHA)-stimulated lymphocytes were predominantly nucleolonemal with 74.2 +-10.6% granular composition. The qualitative and quantitative distribution of nucleolar granular moieties did not vary significantly between individual cases of lymphoma nor quantitatively between these and nucleoli in PHA-stimulated lymphocytes. These observations lend further credence to the suggestion of the lymphocyte as a common progenitor cell type for the large B and T cell of malignant lymphomas. Some functional similarity of their nucleoli and those of PHA-stimulated lymphocytes in their participation in ribonucleic acid synthesis is implied. Generally compact nucleoli of lymphomas in contrast to nucleolonemal forms of PHA-stimulated lymphocytes may be pathognomonic for large lymphocytic cells undergoing neoplasia. (Author abstract) (37 Refs)

41. PATHOLOGICAL CHARACTERISTICS OF ORAL LYMPHOMAS.

Hashimoto N, Kurihara K
Dept. Oral Pathology, Faculty Dentistry, Kyushu Univ., 3-1-1 Maidashi, Higashi-ku, Fukuoka 812, Japan
J Oral Pathol; 11(3):214-227 1982

Histological characteristics in nine cases of oral extranodal lymphoma, including the T- and B-cell types, are described, and the literature is reviewed. Patients ranged in age from 3 to 87 yr old; 7/9 were male. Clinical diagnoses included sarcoma, chronic infection, carcinoma, malignant lymphoma, maxillary carcinoma, and ulcer. Cases were classified histomorphologically as diffuse histiocytic type, nodular histiocytic type, diffuse poorly-differentiated lymphocyte type, and diffuse undifferentiated (Burkitt's lymphoma) type. The ratio of nodal lymphomas to extranodal lymphomas is not remarkably different between Japan and the West. Extranodal lymphomas are found frequently in the oral region, particularly in Waldeyer's ring, and much less often in the oral cavity. Oral cavity extranodal lymphomas were most often found in the masticatory mucosa. No important differences in age of patients, male to female ratio, or stage were evident between Japanese and Western studies; however, histological types were different, with more histiocytic lymphomas and no Hodgkin's disease reported in Japan. (47 Refs)

42. COMPUTED TOMOGRAPHY, ULTRASOUND AND LYMPHOGRAPHY IN THE DIAGNOSIS OF MALIGNANT LYMPHOMA.

Magnusson A, Hagberg H, Hemmingsson A, Lindgren PG
Dept. Diagnostic Radiology, Univ. Hosp., S-75014 Uppsala, Sweden
Acta Radiol [Diagn] (Stockh); 23(1):29-35 1982

Lymphographic findings were compared with the results at histopathology in 42 laparotomized patients with malignant lymphoma. Of 12 patients with lymphographically suggested lesions in normal-sized lymph nodes, only one had pathologic changes at histologic examination. Computed tomography gave a better idea of the extent of the disease than lymphography. Moreover, CT had an equal diagnostic accuracy as lymphography for demonstrating enlarged para-aortic lymph nodes. CT should therefore be able to replace lymphography in examination of malignant lymphoma. Ultrasound had the same diagnostic accuracy as CT regarding the upper and middle abdomen but not in the lower abdomen. Ultrasound is of special value in thin patients and when guided needle biopsy is required. (Author abstract) (25 Refs)

43. SCINTIGRAPHIC INVESTIGATIONS WITH 57CO-BLEOMYCIN AND 67GA-CITRATE IN PATIENTS WITH MALIGNANT LYMPHOMAS.

Brykalski D, Fajndt S, Studniarek M, Surma M, Wiankowski H, Kosmider A
Zaklad Medycyny Nuklearnej i Radiologii, AM w Lodzi, ul. Sterlinga 5, 91-425 Lodz, Poland
Pol Przegl Radiol; 45(6):343-347 1981

The diagnostic value of 57Co-bleomycin scintigraphy in determining the extent of the pathological process was studied and compared with that of 67Ga-citrate in 81 patients with malignant lymphomas. Hodgkin's disease in 14 men and 17 women was clinically diagnosed, and non-Hodgkin's lymphoma in 22 men and 28 women. The sensitivity of the 57-Ga-citrate scintigraphy was found to be 70%, its specificity 72%. The sensitivity and specificity of the 57Co-bleomycin scintigraphy were 75% and 83%, respectively. The superiority of 57Co-bleomycin scintigraphy over 67Ga-citrate was particularly evident in the detection of lesions in the regions of the head, abdomen and pelvis. (18 Refs) (In POL)

44. IN SITU IDENTIFICATION AND ENUMERATION OF HELPER T LYMPHOCYTES IN CUTANEOUS MALIGNANT LYMPHOMAS BY DIPEPTIDYL-PEPTIDASE IV (DPP IV).

Sterry W, Steigleder GK, Goos M, Meisternst E
Dept. Dermatology, Univ. Cologne, Cologne, W. Germany
J Cutan Pathol; 9(2):119-120 1982

Demonstration of dipeptidyl-peptidase IV (DPP IV) was used to reproducibly identify helper T lymphocytes in cutaneous malignant lymphoma. In the plaque stage of mycosis fungoides, the majority of lymphocytes showed DPP IV activity. Thus, mycosis fungoides can be regarded as a malignant helper T lymphocyte proliferation. In the tumor state of mycosis fungoides, DPP IV disappeared from most infiltrating lymphocytes. The decrease of DPP IV-positive lymphocytes may correlate with the onset of the tumor stage and may be of prognostic value. (6 Refs)

MALIGNANT LYMPHOMA: CLINICAL IMMUNOLOGY AND IMMUNOTHERAPY

45. DISTRIBUTION OF T-CELL SUBSETS IDENTIFIED BY MONOCLONAL ANTIBODIES IN CELL SUSPENSIONS FROM LYMPH NODE BIOPSIES OF HUMAN B-CELL LYMPHOMAS.

Kvaloy S, Marton PF, Host H, Solheim BG, Godal T
Lab. Immunology, Norwegian Radium Hosp., Montebello, Oslo 3, Norway
Scand J Haematol; 28(4):293-305 1982

The distribution of T-cell subsets has been examined in cell suspensions from lymph node biopsies from 37 non-Hodgkin lymphomas (NHL) of B-cell origin and 8 cases of Hodgkin's disease (HD). T-inducer/helper cells (T4+ cells) and T-suppressor/cytotoxic cells (T8+ cells) were identified by the monoclonal antibodies OKT4 and OKT8, respectively. Compared with reactive lymph nodes the T-cell subset distribution was aberrant in 18/37 (48.6%) of the B-cell lymphomas. The T-suppressor subset was dominating cells in 14/37 (37.8%) and the T-helper subset in 4/37 (10.8%) of the cases examined. In patients with leukemic disease, a concordant T-cell subset distribution in lymph nodes and PBL was observed in five out of six cases. HLA-DR antigen was examined in a selected number of cases with a heteroantiserum. In general, the T-cells from neoplastic tissues expressed an increased percentage of HLA-DR antigen. This was most pronounced in cases with a dominance of T8+ cells, in which the majority of T8+ cells expressed HLA-DR antigen. These findings suggest that an increased proportion of activated T-suppressor cells are present in a proportion of B-cell lymphomas. Possible clinical and biological implications are discussed. (Author abstract) (51 Refs)

46. INFLAMMATORY RESPONSE IN PATIENTS WITH MALIGNANT LYMPHOMAS.

Bambara LM, Corrocher R, Celebrano R, Martinelli L, Chilosi C, De Sandre G
Istituto di Patologia Speciale Medica II, Policlinico Borgo Roma, 37134 Verona, Italy
Haematologica (Pavia); 67(2):207-215 1982

Chemotactic and phagocytic functions of polymorphonuclear neutrophils (PMN) and monocytes were assayed in 11 patients (9 males, 2 females, 18-68 yr old) with Hodgkin's lymphoma (HL) and 11 patients (6 males, 5 females, 46-71 yr old) with non-Hodgkin's lymphoma (NHL) using the skin window test (SWT). Diagnosis was histologically confirmed. All patients were studied at the time of diagnosis and prior to therapy. Results were compared with those obtained from 20 normal volunteers. The main feature of SWT in HL patients was the delayed PMN phase; at 3 hr the mean total number of PMN was 3,880 +-2,510/coverslip, significantly lower than normal. The nadir was observed at 6 hr (7,890 +-5,420/coverslip). The behavior of PMN-phase was rather constant regardless of clinical stage and histological type of disease, except for persistent depression of the number of PMN in one patient. No difference in the morphology of cells compared with the control group was observed using May Grunwald Giemsa staining. In all groups after 12 hr, a few monocytes showed a positivity for leukocyte alkaline phosphatase varying from + to ++. This finding may be the expression of a false positivity due to debris of cells phagocytosed or alternatively represents the transition to macrophages. In patients with either HL or NHL, the positivity for non-specific-esterase (NSE) was more pronounced than in normal controls, even during the first hours of SWT. In 5/10 patients, 40-60% of monocytes were NSE ++ or +++ and 2/10 were NSE ++ or +++ in approx 20% of monocytes at 3 hr. Thus, chemotaxis and the phagocytic process are severely impaired in NHL, particularly in the late stages. (25 Refs)

47. DISTRIBUTION OF INTERCELLULAR, INTRACYTOPLASMIC AND SURFACE IMMUNOGLOBULINS IN TYPE B NON-HODGKIN'S LYMPHOMA: EMPLOYMENT OF INDIRECT IMMUNOFLUORESCENCE IN THE DETECTION OF IMMUNOMORPHOLOGICAL FEATURES.

Pansa E, Risio M, Bernardi A, Griselli B, Funaro A
Lab. Histopathology, Oncology Dept., Ospedale Maggiore di San Giovanni Battista, Torino, Italy
Pathologica; 74(1029):33-45 1982

Immunomorphological patterns of the distribution of surface (SIg) and intracytoplasmic (CIg) immunoglobulins and free intercellular immunoglobulins (Ig) were examined by immunofluorescence (IF) techniques in 43 patients with type B non-Hodgkin's lymphomas and in 19 patients with reactive hyperplasias. In reactive hyperplasia, primary follicles displayed only SIg-positive cells arranged in a 'honeycomb' pattern; secondary follicles were observed in three concentric areas. In lymphocytic lymphoma (4 cases), the honeycomb pattern was usually observed; the pattern was evenly distributed on the node surface. Very few cells displayed cytoplasmic positivity. Immunocytomas (5 cases) showed diffuse, variously intense SIg-positivity; numerous CIg-positive cells were scattered throughout the preparation. Diffuse centrocytic, centroblastic/centrocytic, and centroblastic lymphomas displayed alternate honeycomb and reticulum areas, interspersed with completely negative areas. Few CIg-positive cells were observed. Monoclonality was seen in two cases. Follicular forms observed in 16 cases of centroblastic/centrocytic lymphoma were usually IF-negative. Very weak honeycombs were detected. Some av size CIg-positive cells were noted in six cases. Completely negative areas interspersed with fields of limited size that displayed weak reticulum or honeycomb positivity in lymphoblastic lymphomas (4 cases). CIg-positive cells were uniformly distributed with monoclonality in two cases. Characteristics of immunoblastic lymphoma (2 cases) were attributable to CIg-positive cells. Probable monoclonality was observed in two cases. (26 Refs)

48. THE CELL POPULATION IN THE CUTANEOUS INFILTRATE OF MYCOSIS FUNGOIDES: IN SITU STUDIES USING MONOCLONAL ANTISERA.

Holden CA, Morgan EW, MacDonald DM
(c/o MacDonald) Dept. Dermatology, Guy's Hosp., St. Thomas' St., London SE1 9RT, England
Br J Dermatol; 106(4):385-391 1982

T cell antigens were studied in cutaneous sections from five patients with mycosis fungoides (MF). The method allowed cell counting to be undertaken for each monoclonal antiserum. OKT3 (pan T cell) antiserum confirmed the predominantly T lymphocytic nature of the infiltrate, labeling the majority of infiltrating cells. OKT4 (helper/inducer) antiserum positively labeled 90% of the lymphocytes identified as OKT3+. OKT8 (suppressor) antiserum marked only single or small groups of dermal lymphocytes, which comprised 24% of the cells identified as T lymphocytes. OKT6 (anti-Langerhans) showed positive labeling of dendritic cells in the epidermis and dermis. Fewer positively labeled epidermal dendritic cells were observed in sections from patients receiving PUVA, but no difference was found in the number of OKT6 positive dermal cells. The ratio of helper to suppressor cells in the dermal infiltrate significantly exceeded the normal circulating ratio. (Author abstract) (16 Refs)

49. SUBTYPES OF CUTANEOUS T-CELL LYMPHOMA DEFINED BY EXPRESSION OF LEU-1 AND IA.

Wood GS, Deneau DG, Miller RA, Levy R, Hoppe RT, Warnke RA
Dept. Pathology, Stanford Univ. Medical Center, Stanford, CA, 94305
Blood; 59(5):876-882 1982

Monoclonal antibodies were used to characterize immunohistologically the expression of cellular antigens in 25 patients with cutaneous T-cell lymphoma (CTCL). Although all cases expressed the Leu-2a-/Leu-3a+ immunophenotype characteristic of helper T cells, four subtypes were defined based on variable expression of Leu-1 and Ia. In individual patients, the immunophenotype was constant irrespective of body compartment sampled or interim therapy. Ia+ non-T-cells typically constituted one-third of the cellular infiltrate. Along with neoplastic cells, Ia+/T6+ dendritic cells were observed within Pautrier microabscesses, dermis, and individually throughout the epidermis. It will be important to determine if different CTCL immunophenotypes represent different biologic subsets of disease or have prognostic relevance. Prospective studies will be facilitated by single- and double-label immunohistologic techniques that allow the simultaneous evaluation of cellular antigen expression and architectural detail. (Author abstract) (30 Refs)

50. THE USE OF A DOUBLE-LABEL IMMUNOPEROXIDASE MONOCLONAL ANTIBODY TECHNIQUE IN THE INVESTIGATION OF PATIENTS WITH MYCOSIS FUNGOIDES.

MacKie RM, Turbitt ML
Dept. Dermatology, Univ. Glasgow, Anderson College Building, 56 Dumbarton Road, Glasgow G11 6NU, Scotland
Br J Dermatol; 106(4):379-383 1982

Using a double-labeling immunoperoxidase technique and monoclonal antibodies raised against T helper and T suppressor cells and Langerhans cells, we have found that the clinically involved skin of 17 mycosis fungoides (MF) patients shows an increase in number of Langerhans cells which are in contact with T helper lymphocytes. T suppressor lymphocytes are also present, but are generally seen singly and situated at a distance from the T helper/Langerhans cell clusters. (Author abstract) (9 Refs)

MALIGNANT LYMPHOMA: CHEMOTHERAPY

51. COMBINATION CHEMOTHERAPY FOR PATIENTS WITH RELAPSED MALIGNANT LYMPHOMA USING METHYL-GAG AND TENIPOSIDE (VM-26).

Warrell RP, Straus DJ, Young CW
Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Cancer Treat Rep; 66(5):1121-1125 1982

We treated 45 patients with advanced malignant lymphoma, using a combination of methyl-GAG and teniposide (VM-26). All patients had received extensive prior treatment with combination chemotherapy with or without irradiation. Both methyl-GAG (600 mg/m2) and VM-26 (100 mg/m2) were administered on Days 1 and 8 of the treatment protocol and, in responding patients, every 2 wk thereafter. Partial responses occurred in 6 of 12 patients with Hodgkin's disease and in 10 of 31 patients with non-Hodgkin's lymphoma. The median duration of response for all patients was 3-1/2 mo (range 1.5-11). There were moderate toxic effects, including nausea, myalgia, weakness, and myelosuppression. Relative to our recent experience with methyl-GAG as a single agent, the addition of VM-26 to methyl-GAG did not produce a superior rate or duration of response in similar, heavily pretreated patient populations with malignant lymphoma; however, the combination caused considerably more myelotoxicity. We conclude that the use of VM-26 with methyl-GAG in this dose schedule offers no advantage over single-agent therapy. Methyl-GAG, when administered on a biweekly schedule, is effective and well-tolerated. This agent should be considered for incorporation into chemotherapy protocols for the therapy of previously untreated patients with malignant lymphoma. (Author abstract) (13 Refs)

52. INTENSIVE CHEMOTHERAPY FOLLOWED BY BONE MARROW AUTOGRAFT IN THE TREATMENT OF MALIGNANT LYMPHOMAS REFRACTORY TO CLASSICAL CHEMOTHERAPY: RESULTS AND PROJECTIONS.

Stryckmans P, Debusscher L, Delforge A, Bron D, Vanhaelen C, Ronge-Collard E, Bieva C, Loos M
Service de Medecine, Institut Jules Bordet, Brussels, Belgium
Rev Med Brux; 3(4):255-260 1982

Patients with nonHodgkin's lymphoma (NHL) who do not respond to conventional chemotherapy often respond to intensive chemotherapy, achieving complete remission in 5-20% of cases even though complete remissions are of short duration. Intensive chemotherapy followed by bone marrow grafts have shown much more promise in obtaining complete remissions of longer duration. Problems associated with immunological responses to donor marrow can be avoided by the use of autologous marrow. This type of treatment should be reserved for patients who have the worst prognosis. Factors that warrant autologous transplants include are medullary infiltration, male patients, general symptoms, and the existence of a large abdominal mass. Burkitt's lymphoma and lymphoblastic lymphoma are NHL that have the worst prognosis. Bone marrow should be taken as soon as possible in order to avoid the cumulative deleterious effects of chemotherapy used against the lymphoma, and the marrow should be free of medullary tumor infiltration. In the presence of tumor infiltration, the marrow can be taken later if conventional chemotherapy leads to complete remission. Clinical, immunological, and physical methods are now being tested to rid grafts of tumor cells. (31 Refs) (In FRE)

53. CLINICAL-MORPHOLOGICAL CHARACTERISTICS OF MYCOSIS FUNGOIDES TREATED WITH PROSPIDIN IN COMBINATION WITH CORTICOSTEROID HORMONES.

Tevzadze MSm
Dept. Dermatology, Res. Inst. Skin-Venereal Diseases, Tbilisi, USSR
Vestn Dermatol Venerol; (4):10-14 1982

Therapeutic efficacy of prospidin (3,000-3,500 mg) in combination with corticosteroid hormones was studied in 60 patients with mycosis fungoides (MF). Clinical improvement was achieved in 84% of the patients. Histological and electron microscope examination of MF lesions showed that treatment caused marked decrease of the acanthosis. Mild dermal infiltrates consisted of mature histiocytes and lymphocytes without marked atypia. (14 Refs) (In RUS)

MALIGNANT LYMPHOMA: MULTIMODAL THERAPY

54. COMBINATION CHEMOTHERAPY (CVP OR CHOP)-RADIOTHERAPY APPROACH IN EARLY STAGE NON-HODGKIN'S LYMPHOMAS.

Comella P, Scoppa G, Abate G, Comella G, Apice G, Castello G, Pergola M, Giordano GG, Coucourde F, Zarrilli D
Istituto dei Tumori, Cappella dei Cangiani, 80131 Napoli, Italy
Tumori; 68(2):137-142 1982

From January 1978 to December 1980, 42 patients with early stage non-Hodgkin's lymphoma other than of the gastrointestinal tract were treated with radiotherapy and combination chemotherapy. Eighteen patients in Stage I were submitted to locally extended-field radiotherapy up to a mean dose of 48 Gy with a Co60 source and, after a 3-wk rest period, to six cycles of combination chemotherapy. Twenty-four patients in Stage II received three cycles of combination chemotherapy before and after irradiation, the same as for Stage I. Combination chemotherapy consisted of cyclophosphamide, vincristine and prednisone (CVP) for 15 cases with favorable histology (3 NWDL, 1 NPDI, 11 DWDL), whereas it included cyclophosphamide, adriamycin, vincristine and prednisone (CHOP) for 27 cases with unfavorable histology (20 DPDL, 3 DM, 4 DH). Complete remission (CR) was achieved in 35/42 (83%) patients, with a highly significant difference between Stage I (100%) and Stage II (71%). After 42 mo of follow-up, the probability of survival for all patients was 72%. Survival was better for Stage I (88%) than for Stage II (68%) and for favorable histology (87%) as compared to unfavorable histology (70%). Furthermore, survival was highly influenced by response to therapy. Indeed, actuarial survival rate for CR was 91% as compared to a median survival time of 10.2 mo for the remaining patients. Four patients, all with poor histology, relapsed after 5-24 (mean 11) mo of CR. Only one of them had an extension in extranodal sites and eventually died, despite the salvage treatment utilized. In our experience, locally extended-field irradiation combined with chemotherapy gave a high proportion of CR and seemed to prevent relapses, particularly in extranodal sites. (Author abstract) (32 Refs)

55. RESULTS OF A STUDY ON THE TREATMENT OF NON-HODGKIN'S LYMPHOMA USING A COMBINED MODALITY APPROACH (MEETING ABSTRACT)

Plaumann L, Havemann K, Diehl V, Gassel WD, Schumacher K, Langer B, Hassenstein E, Heb K
Abteilung Hamatologie/Onkologie und Abteilung fur Strahlentherapie, Medizinischen Hochschule Hannover, Karl-Wiechert-Allee 9, D 3000 Hannover 61, W. Germany
J Cancer Res Clin Oncol; 103(Suppl):A15 1982

The results presented were obtained from a current multicenter randomized treatment study on high-grade, previously untreated non-Hodgkin's lymphoma (NHL), stages II to IV, in 43 patients. All patients (ages 25 to 75 years) received from 6 to 9 courses of chemotherapy using a modified CHOP regime (CVC (cyclophosphamide) 750 mg/m2 IV over 21 days; ADM (adriamycin) 50 mg/m2 IV over 21 days; VCR (vincristine) 1.4 mg/m2 IV over 21 days; Prednisolone 100 mg oral days 1-4, 25 mg oral day 5). After the fourth course of chemotherapy, they received 'involved field' radiotherapy of all primary manifestations using 25 GyHD. One group of patients was additionally intervenously treated with 3 mg/m2 Corynebacterium parvum (Coparvax) on day 6 of each chemotherapy course. After seven and ten therapeutic courses, respectively, patients were restaged. Patients with complete remission (CR) received maintenance therapy consisting of COP in increasing intervals over a period of two years. At the time of evaluation, Group 'A' (with C parvum) consisted of 21 patients, and Group 'B' (no C parvum) of 23 patients. There was no statistically significant difference between A and B. Since the addition of C parvum to the regimen did not have any demonstrable effect, groups A and B were pooled for the analysis. An overall response rate was 72% with 64% in CR. Sixty-nine percent of centroblastic NHL, 85% of immunoblastic NHL and 53% of lymphoblastic NHL went into CR. The latter group often showed a progression, not seldom transforming into therapy-resistant ALL. During the time of follow-up, only one patient in CR suffered a relapse. We conclude that the chosen scheme of therapy is highly effective in centro- and immunoblastic

NHL. There was only moderate treatment related toxicity and most patients were treated on an out-patient basis. (no Refs)

56. GASTRIC LYMPHOMA: AN ANALYSIS OF 28 CASES (MEETING ABSTRACT)

Shimm D, Dosoretz D, Harris N, Linggood R, Wang CC
Department of Radiation Medicine and Pathology, Massachusetts General Hospital and Harvard Medical School, Boston, MA, 02114
Am J Clin Oncol; 5(2):131 1982

A computer search of tumor registry, hospital chart, and radiotherapy records from 1963 to 1980 identified 41 patients with gastric lymphoma. Thirteen had gastric involvement as a late manifestation of widespread lymphoma and are excluded from analysis. The remaining 28 were subjected to actuarial survival analysis. Overall 5-year survival was 54%; 5-year NED (no evidence of disease) survival was 50%. Twenty patients received postoperative radiotherapy (RT) to the gastric bed and upper paraaortic nodes (mean 34 GY) with 60% 5-year survival, compared to 24% 5-year survival for those treated with surgery alone. Widely disseminated disease was the usual mechanism of failure. Four abdominal failures were seen, three in patients who had received RT; no patient receiving over 40 Gy had failure in the abdomen. Factors important for 5-year survival were regional nodal status (82%, negative nodes; 15%, positive nodes) and resection margins and serosa (100% , uninvolved; 12%, involved). Seven patients had uninvolved nodes, margins, and serosa and all are NED with a median follow-up of 7 years; three received no RT. Surgical and radiotherapeutic complications included postoperative sepsis in two, enteritis in one, and osteomalacia in one. Review of pathologic material is pending; significance of histology will be discussed. Gastric lymphoma without involvement of serosa, margins, or regional nodes can be cured by resection followed by RT. Patients with any of these poor prognostic factors should be considered for additional systemic chemotherapy because of their high risk of dissemination. (no Refs)

MALIGNANT LYMPHOMA: CASE REPORTS

57. EVOLUTION OF INFECTIOUS MONONUCLEOSIS INTO EPSTEIN-BARR VIRUS CARRYINC MONOCLONAL MALIGNANT LYMPHOMA.

Abo W, Kamada M, Motoya T, Aya T, Nakao T, Takada K, Imamura M, Iwanga M, Yano S, Osato T
(c/o Osato) Dept. Virology, Cancer Inst., Hokkaido Univ. Sch. Medicine, Sapporo 060, N15 W7, Japan
Lancet; 1(8284):1272-1276 1982

A monoclonal malignant lymphoma was diagnosed in a 30-mo-old Japanese boy, who, since the age of 12 mo, had had chronic, recurrent infectious mononucleosis manifested by repeated episodes of severe cough and high fever accompanied by marked lymphadenopathy and hepatosplenomegaly and high serum Epstein-Barr virus (EBV) antibody titers. The diagnosis of Burkitt's lymphoma was made when a cervical lymph-node biopsy specimen revealed massive proliferation of immature B-cells with starry-sky histiocytes. These lymph-node cells were characterized by a translocation between chromosomes 10 and 17. There were approx 9 EBV genome-equivalents per cell. Most cells were positive for nuclear antigen (EBNA); early antigen (EA) and viral capsid antigen (VCA) were also detected. The presence of EBV was supported by the finding that the cell-free lymph-node extract transformed cord-blood lymphocytes into EBNA-positive blast cells. The proportion of EA-positive and VCA-positive cells increased rapidly in culture for 24 hr, then the positive cells degenerated rapidly and completely. The cells also contained numerous herpes-type virus particles. The child improved considerably with cytostatic treatment and has been in remission for 2 yr. (Author abstract) (23 Refs)

MALIGNANT LYMPHOMA: SELECTED REPORTS ON ETIOLOGY AND EPIDEMIOLOGY

58. DIFFUSE, UNDIFFERENTIATED NON-HODGKINS LYMPHOMA AMONG HOMOSEXUAL MALES --- UNITED STATES.

Ziegler JL, Wagner G, Greenspan JS, Shillitoe EJ, Greenspan D, Beckstead J, Cassavant C, Abrams D, Chan W, Silverman S, Lozada F, Drew L, Rosenbaum E, Miner R, Mintz L, Gershow J, Weiss R, Yamamoto K, Chick K, Dritz S, Austin D, Chin J, McGuire W, Iossifides I, Francis BJ, Costa J
Veterans Admin. Medical Center, San Francisco, CA
MMWR; 31(21):277-279 1982

Four cases of diffuse, undifferentiated non-Hodgkins lymphoma (DUNHL) are described, with a discussion of the epidemic of Kaposi's sarcoma, Pneumocystis carinii, and other opportunistic infections (KSOI) among homosexual males and the possible relationships between the two disorders. All four patients were homosexual males living in San Francisco; all had used various drugs, and had had infections such as hepatitis B, anal warts, gonorrhea, and syphilis. The association of DUNHL and KSOI suggests that more than one kind of tumor may be involved in the KSOI syndrome. (15 Refs)

59. FAMILIAL T-CELL LYMPHOBLASTIC LYMPHOMA: ASSOCIATION WITH VON RECKLINGHAUSEN NEUROFIBROMATOSIS AND GARDNER SYNDROME.

Kaplan J, Cushing B, Chang CH, Poland R, Roscamp J, Perrin E, Bhaya N
Children's Hosp. Michigan, 3901 Beaubien Blvd., Detroit, MI, 48201
Am J Hematol; 12(3):247-250 1982

A family is described in which three of seven siblings developed a T-cell lymphoblastic lymphoma. Tumor cells formed rosettes with sheep erythrocytes, lacked surface Ig, and expressed human T- but not B-lymphocyte antigens. They lacked the enzyme terminal transferase suggesting a lymph node rather than thymic T-cell origin. Autopsy findings supported this conclusion. All three sibs, like their father, had numerous cafe au lait spots indicative of Von Recklinghausen neurofibromatosis. One child had a sc fibroma, and another had multiple colonic polyps and exostoses characteristic of Gardner syndrome. Both are autosomal dominant conditions known to predispose to malignancies. The genetic factors responsible for these conditions may also predispose to the development of 'post-thymic' T-cell lymphoblastic lymphoma. (Author abstract) (10 Refs)

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HODGKIN'S DISEASE: DIAGNOSIS AND STAGING

1. SERUM ALPHA-1-ACID-GLYCOPROTEIN, HAPTOGLOBIN AND C3 IN HODGKIN'S DISEASE. A COMPARISON WITH OTHER ACUTE-PHASE INDICATORS.

Gobbi PG, Merlini G, Parrinello GA, Cavalli P, Ascari E
Istituto di Patologia Medica I, Universita di Pavia, Policlinico S. Matteo, I-27100 Pavia, Italy
Acta Haematol (Basel); 67(4):255-262 1982

One hundred seven determinations of alpha1-acid-glycoprotein (alpha1S), haptoglobin (Hp) and complement fraction 3 (C3) were made in 85 consecutive patients with Hodgkin's disease, both in acute phase (77 measurements) and in complete remission (30 measurements). Only alpha1S and Hp showed much higher levels in untreated disease than in remission, and elevation of alpha1S in activity of the disease is correlated to advanced stages and - less significantly - to severe histology. The ability of alpha1S, Hp and C3 to discriminate between activity and remission was compared with that of erythrocyte sedimentation rate (ESR), alpha2-globulinemia (alpha2), fibrinogenemia (Fb), plasma copper (Cu) and iron (Fe), all data being collected at the same point in time in each patient. The well-known discrimination ability of combined Cu and Fe (75%) can be further improved by alpha1S (81%) much more than by Hp, C3, ESR, alpha2, and Fb singly computed and nearly up to the maximum allowed by the eight indexes together (82%). (Author abstract) (23 Refs)

2. ADENOSINE DEAMINASE ACTIVITY IN HODGKIN'S DISEASE.

Muller G, Krug K, Kruger W, Richter V, Rassoul F
II. Medizinische Klinik und Poliklinik, Martin-Luther-Universitat, Halle-Wittenberg, Leninallee 2, DDR-402 Halle, E. Germany
Klin Wochenschr; 60(6):317-318 1982

The activity of adenosine deaminase (ADA) (EC3.5.4.4) was determined in the blood plasma, erythrocytes, and lymphocytes of 23 patients with Hodgkin's disease and partly also in 99 control subjects. The enzyme activities were measured using adenosine as substrate and by analysis of ammonia. No correlation was found between the ADA activities in lymphocytes, erythrocytes, and blood plasma. The lymphocytes of the patients revealed lower ADA activities (U/g protein) than the lymphocytes of control subjects. The ADA activity is not reduced in plasma or erythrocytes. The lower activities of ADA in the lymphocytes of patients may be related to the impaired cell-mediated immunity of the Hodgkin's disease. (Author abstract) (14 Refs) (In GER)

3. THE LIVER IN HODGKIN'S DISEASE - II. HISTOPATHOLOGIC FINDINGS.

Skovsgaard T, Brinckmeyer LM, Vesterager L, Thiede T, Nissen NI
Dept. Medicine and Pathology, Finsen Inst., Copenhagen 2100 O, Denmark
Eur J Cancer Clin Oncol; 18(5):429-435 1982

Histopathologic findings in 459 liver biopsies performed in 308 patients with Hodgkin's disease were reviewed. Typical Hodgkin infiltrates were found in only 11/459 biopsies (2.4%) and infiltrates suspect for Hodgkin's disease in only 8/459 (1.7%), whereas unspecific changes were more common. Lymphocytic infiltration was seen in 47% of the biopsies and focal necrosis in 19%. No correlation could be demonstrated between unspecific changes and clinical characteristics, including prognosis. (Author abstract) (17 Refs)

HODGKIN'S DISEASE: CLINICAL IMMUNOLOGY AND IMMUNOTHERAPY

4. DIMINISHED AUTOLOGOUS MIXED LYMPHOCYTE REACTION IN PATIENTS WITH HODGKIN DISEASE: EVIDENCE FOR NON-T CELL DYSFUNCTION.

Zamkoff KW, Dock NL, Kurec AS, Davey FR
Dept. Medicine, Upstate Medical Center, 750 East Adams St., Syracuse, NY, 13210
Am J Hematol; 12(4):327-335 1982

In the autologous mixed lymphocyte reaction (AMLR), T lymphocytes are stimulated to proliferate by autologous non-T mononuclear cells. In five untreated patients with Hodgkin disease, the AMLR was diminished. In addition, in the same five patients, T cell response to PHA was inhibited by a cell in the non-T cell fraction, the response of non-T cells to PWM was diminished, and there was a diminished ability of the non-T cell population to stimulate in allogeneic MLR. However, the response of T cells from patients with Hodgkin disease to allogeneic antigen was normal. The AMLR and allogeneic MLR were then studied in an additional five untreated patients before and after monocyte depletion of the stimulating non-T mononuclear cell population. In this second group of Hodgkin disease patients, the AMLR was again diminished when T cells were incubated either with non-T cells or non-T cells depleted of monocytes. In the Hodgkin patients, monocyte depletion did not alter the T cell response in the AMLR. In the controls, monocyte depletion greatly diminished the proliferative response. The diminished AMLR in untreated Hodgkin disease patients may be the result of a failure of adequate monocyte stimulation of autologous T cells. (Author abstract) (20 Refs)

5. TISSUE T-LYMPHOCYTES IN UNTREATED HODGKIN'S DISEASE. MORPHOLOGIC AND FUNCTIONAL CORRELATIONS IN SPLEENS AND LYMPH NODES.

Baroni CD, Ruco L, Uccini S, Foschi A, Occhionero M, Marcorelli E
IV Cattedra di Anatomia ed Istologia Patologica, Universita di Roma, 00161 Roma, Italy
Cancer; 50(2):259-268 1982

In the present study the number of E-RFC and the in vitro response to PHA and ConA were determined for lymphocytes obtained from spleens and lymph nodes of untreated HD patients. The results were correlated with tissue involvement and with the histological pattern of the disease. Our investigation has revealed; (1) involved spleens and lymph nodes contained a higher percentage of T-lymphocytes than uninvolved tissues. The difference was statistically significant for lymph nodes. (2) A statistically significant correlation was not found between T-lymphocyte numbers and histology. (3) Lymphocytes from uninvolved spleens were significantly more reactive to both mitogens than cells from involved spleens and control non-neoplastic spleens as well. (4) Similar results were obtained with lymph node lymphocytes; however a significant difference was observed only when cells were stimulated with ConA. (5) The difference in proliferative response between uninvolved and involved tissues was maximally expressed in MC and progressively decreased in NS and LP. (6) T-cell enrichment does not alter the difference between uninvolved and involved spleens. (7) Cells from uninvolved and involved spleens, cultured for 24 hr, maintained unchanged their proliferative capacity. In this study evidence is provided that in HD T-lymphocytes from uninvolved tissues are characterized by an increased reactivity to mitogens, whereas cells from involved tissues are normally responsive. (Author abstract) (37 Refs)

6. IMMUNITY AND HYPERSENSITIVITY IN HODGKIN'S DISEASE.

Leoni P, Marchegiani G, Montillo M, Centurioni R, Montroni M, Danieli G

Istituto di Patologia Speciale Medica e Metodologica Clinica, Universita di Ancona, Ancona, Italy

Minerva Med; 73(20):1361-1369 1982

Some immunological parameters (absolute count and percentage of lymphocytes, E rosettes and lymphocytes with S immunoglobulin (S-Ig)) were studied in 47 patients with Hodgkin's disease (HD). The percentages of lymphocytes were found to be 33% in Stage I, 26% in II, 21% in III and 20.7% in IV; 46% in lymphocyte predominant (LP) type, 22.3% in nodular sclerotic (NS) Type, 27.6% in mixed cellular (MC) Type and 24.6% in lymphocyte depleted (LD) Type. The percentages of E rosettes were 58% in Stage I, 50.8% II, 52% in III and 50% in IV; 35% in LP Type, 53.1% in NS Type, 46.6% in MC Type and 45.5% in LD Type. The percentages of lymphocytes with S-Ig were 17% in Stage I, 32% in II, 35.5% in III and 24.3% in IV; 22.9% in LP Type, 31.7% in NS Type, 30.5% in MC Type and 38% in LD Type. Functional and anatomic depression of the T-cell system is prevalent or exclusive in patients with Stages III and IV of HD of MC and LD Type. Studied on immunological changes and their causes in patients with HD are reviewed. (111 Refs) (In ITA)

HODGKIN'S DISEASE: CHEMOTHERAPY

7. FIVE YEARS' EXPERIENCE WITH CHLVPP: EFFECTIVE LOW-TOXICITY COMBINATION CHEMOTHERAPY FOR HODGKIN'S DISEASE.

Dady PJ, McElwain TJ, Austin DE, Barrett A, Peckham MJ

(c/o McElwain) Lymphoma Unit, Div. Medicine and Radiotherapy, Inst. Cancer Res., Sutton, Surrey, England

Br J Cancer; 45(6):851-859 1982

Since 1975, 191 patients with Hodgkin's disease have been treated with a combination of chlorambucil, vinblastine, procarbazine and prednisolone (ChlVPP). Complete remission rates were 73% for previously untreated patients, 91% for patients previously treated with radiotherapy and 55% for patients previously treated with chemotherapy. In 59 patients with advanced disease who received no other treatment, a 5-yr survival rate of 66% was comparable with that achieved by more toxic mustine-containing combinations. ChlVPP has few side effects, is easily given to outpatients, and can be combined with elective radiotherapy in selected patients. (Author abstract) (20 Refs)

8. PROGNOSTIC FACTORS IN COPP-TREATED PATIENTS WITH HODGKIN'S DISEASE.

Gassmann W, Perenyi L, Schmitz N, Kayser W, Prolle H, Loffler H

II. Medizinische Klinik und Poliklinik, Christian-Albrechts-Universitat Kiel, Metzstr. 53, D-2300 Kiel, W. Germany

Blut; 44(6):339-348 1982

In a recently published review of the literature we came to the conclusion that the Ann-Arbor staging classification is of limited prognostic value for chemotherapy of Hodgkin's disease. Four risk factors accounted for impaired complete remission rates: Stage IVB, lymphocyte depletion or not classifiable histologic type, previous chemotherapy, and older age. Fifty-eight evaluable patients were treated with COPP; 23 reached a complete remission (40%). Disease-free survival was 31%, overall survival 49% after 5 yr. Besides the known risk factors, impaired bone marrow function (leukocyte counts less than 4 x 10(9)/l, platelet counts less than 100 x 10(9)/l) at the start of therapy was associated with poor treatment results: none of six patients achieved a complete remission. Eleven of 16 patients with no and 11 of 23 patients with one risk factor achieved a complete remission, as did only one patient with more than one risk factor. Survival rates after 30 mo were: 87% with no, 66% with one, 36% with two, and 13% with more than two risk factors. We can conclude from our results that the prognosis of patients undergoing chemotherapy for Hodgkin's disease depends on the number of risk factors. (Author abstract) (63 Refs)

9. GONADAL FUNCTION AFTER COMBINATION CHEMOTHERAPY FOR HODGKIN'S DISEASE IN CHILDHOOD.

Whitehead E, Shalet SM, Morris Jones PH, Beardwell CG, Deakin DP

(c/o Shalet), Christie Hosp. and Holt Radium Inst., Wilmslow Road, Manchester M20 9BX, England

Arch Dis Child; 57(4):287-291 1982

The effect of quadruple chemotherapy (mustine, vincristine, procarbazine and prednisolone) on gonadal function was investigated in 15 males and 2 females treated for Hodgkin's disease during childhood. The two females have regular menstrual cycles with evidence of ovulation in one. Twelve of the males have shown normal progression of pubertal development since completing their treatment. Nine out of 10 late pubertal or adult subjects had small testes but only one developed gynecomastia. All four prepubertal subjects had normal basal and peak gonadotrophin responses to luteinizing hormone-releasing hormone. Nine of the 12 subjects studied during puberty or adulthood had either an increased basal serum follicle-stimulating hormone (FSH) level or an exaggerated FSH response to luteinizing hormone-releasing hormone. Each of the six males who provided semen for analysis was azoospermic after an interval of between 2.4 and 8 (mean 5.3) yr after completion of treatment. We conclude that severe testicular damage is common after treatment with mustine, vincristine, procarbazine, and prednisolone in childhood. The germinal epithelium is particularly vulnerable and the resultant azoospermia is likely to be irreversible. The Leydig cells are less susceptible to cytotoxic-induced damage. Pubertal development is normal and there is no indication for androgen replacement therapy. (Author abstract) (20 Refs)

HODGKIN'S DISEASE: RADIOTHERAPY

10. PATTERNS OF RELAPSE FOLLOWING RADIOTHERAPY FOR HODGKIN'S DISEASE.

Yarnold JR, Jelliffe AM, Hudson GV
(c/o Jelliffe) Dept. Radiotherapy and Oncology, Middlesex Hosp., London, England
Clin Radiol; 33(2):137-140 1982

A study of the relationship between bulk disease and sites of relapse has been undertaken in 95 patients treated by radiotherapy for early stage Hodgkin's disease. All patients were investigated and treated according to protocols of the British National Lymphoma Investigation. In a group of 80 pathologically staged patients the pattern of relapse in 39 patients confirms an association between recurrence and sites of bulk involvement in the mediastinum, neck and axilla. Bulk disease predisposes to recurrence by virtue of local failure inside the treatment vol as well as marginal recurrence. A small number of patients relapsed initially in sites that were irradiated prophylactically. (Author abstract) (8 Refs)

11. HYDROCELE FOLLOWING TREATMENT FOR HODGKIN'S DISEASE.

Duffey P, Campbell EW, Wiernik PH
(c/o Wiernik), Baltimore Cancer Res. Program, 22 South Greene St., Baltimore, MD, 21201
Cancer; 50(2):305-307 1982

Thirteen Hodgkin's disease patients developed hydrocele after treatment with radiotherapy (12 patients) or chemotherapy (1 patient). An additional patient developed testicular swelling following radiotherapy and chemotherapy. Eleven of 13 patients were staged with laparotomy (9 initially, 2 at restaging) which included pelvic and aortic node biopsies prior to development of hydrocele. Five of the patients developed radiation-related pericarditis. These data suggest that staging and treatment of Hodgkin's disease may disrupt pelvic lymphatic flow and lead to hydrocele formation. The high incidence of treatment-related pericarditis may suggest unusual sensitivity to radiation in this group of patients. (Author abstract) (3 Refs)

HODGKIN'S DISEASE: MULTIMODAL THERAPY

12. THERAPY FOR HODGKIN'S DISEASE IN CHILDREN.

Lobo-Sanahuja F, Garcia I, Jimenez E, Jimenez R, Camacho A, Vargas G
Servicio de Oncologia, Hospital Nacional de Ninos, Apartado 10105, San Jose, Costa Rica
Sangre (Barc); 27(1):26-38 1982

A study was carried out to compare the results attained from the use of cobalt radiation therapy plus cyclophosphamide, vincristine, procarbazine and prednisone (COPP) chemotherapy with those attained by irradiation alone in children with Hodgkin's disease. The percentage of remissions, their duration, and the survival were evaluated in three groups of patients treated with two different protocols started in January 1971 and 1972 and closed in December 1978. Group 1 was comprised of 15 patients without systemic symptoms who had been subjected to laparotomy. Of them, eight were in Stage I, two in Stage II, and five in Stage III; they all received irradiation alone. Total remission was achieved in 100% with mean duration of 38 months. Remission was maintained in 47% of the cases, while 53% relapsed. These last achieved second remission with GOPP, but 3 patients died, 12 being alive, with 84-month survival in 45% of cases. Group 2 included 10 patients in Stages I to III without systemic symptoms. These patients were treated with irradiation plus COPP chemotherapy and achieved complete remission with 31-months mean survival. Group 3 was comprised of 13 patients, 8 in Stage III-B and 5 in Stage IV; they received chemotherapy and radiation therapy, 85% of remissions being attained. Relapse occurred in 18% of the cases in this group, ie two patients, of whom one died and the other attained a second remission with ABVPP (adriamycin, bleomycin, vinblastine, procarbazine and prednisone) chemotherapy. Within this group, 52% of the patients have 84 month survival. The mortality of the series as a whole has been 16% (6 patients). It was concluded that chemotherapy plus 60Co irradiation yields better results than cobalt irradiation alone. (Author abstract) (28 Refs) (In SPA)

HODGKIN'S DISEASE: CASE REPORTS

13. RENAL MANIFESTATIONS IN HODGKIN DISEASE. TWO CASE-REPORTS WITH A REVIEW OF THE MEDICAL LITERATURE.

Rossi JF, Dubois A, Brunel M, Janbon C, Vallat G
(c/o Vallat) Clinique Medicale B, Hopital Saint-Eloi, avenue Bertin-Sans, 34059 Montpellier Cedex, France
Sem Hop Paris; 58(24):1471-1475 1982

The authors report on two patients in whom Hodgkin disease was revealed by renal complications: nephrotic syndrome in one patient and renal failure with enlarged kidneys secondary to malignant infiltration in the other. In comparison to other lymphomas, renal infiltration is infrequent in Hodgkin disease. Clinical manifestations of renal infiltration are delayed. Renal failure with enlarged kidneys, which is very uncommon, carries a poor prognosis and is often associated with involvement of the lungs. Nephrotic syndrome in Hodgkin disease may be secondary to one of the three following causes: renal vein compression, renal amyloidosis, or a paraneoplastic syndrome. The latter is the most common cause and is probably ascribable to immunologic disturbances. Among the other complications, infection and the renal consequences of metabolic disorders are mentioned. (Author abstract) (40 Refs) (In FRE)

HODGKIN'S DISEASE: SELECTED REPORTS ON ETIOLOGY AND EPIDEMIOLOGY

14. HODGKIN'S DISEASE IN WESTERN INDIA. REVIEW OF 1082 CASES.

Talvalkar GV, Sampat MB, Gangadharan P
Tata Memorial Hosp., Parel, Bombay-400012, India
Cancer; 50(2):353-359 1982

Hodgkin's disease (HD) had a low overall incidence rate in Bombay when compared to western countries. However, the incidence rate in childhood was quite high. Review of 1,082 cases of Hodgkin's disease recorded at the Tata Memorial Hospital, Bombay, India during a period of 35 yr showed that mixed cellularity, with 54% of the total, was the most frequent histologic subtype and this, together with lymphocyte depleted type formed 68% of all HD. The nodular sclerosis type formed only 9%. A bimodal character of the age pattern with a young age peak in the second decade of life, a male preponderance, a high incidence in childhood, and the predominance of low survival types, are the major features of the disease in India. The current data, which are the largest series reported from Bombay and other parts of India, indicate that the Type-I pattern as described by Correa and O'Conor may be the characteristic feature of the Hodgkin's disease in India. (Author abstract) (23 Refs)

HODGKIN'S DISEASE: REVIEWS

15. EVOLUTION IN THE TREATMENT STRATEGY OF HODGKIN'S DISEASE.

Bonadonna G, Santoro A
Div. Medical Oncology, Natl. Tumor Inst., Milan, Italy
Adv Cancer Res; 36:257-293 1982

Radiation therapy, chemotherapy, new treatment strategies, and prognostic factors and morbidity in relation to treatment strategy for Hodgkin's disease are reviewed. Improvement in treatment results has been achieved at all major research centers. No stage of the disease is beyond cure after the initial treatment program, and even after recurrence following primary irradiation. In the future more attention should be given to the potential of alternating treatments to deal with primary drug resistance. Cyclical or sequential use of non-cross-resistant combinations of agents is likely to improve the cure rate in advanced Hodgkin's disease. New clinical studies should evaluate combined therapy using non-cross-resistant combinations. Treatment should start with chemotherapy, and should be alternated with irradiation. Since nearly one-third of patients with Hodgkin's disease die without evidence of lymphoma at autopsy, it is important to design treatment programs to deal with bacterial infection and complications of therapy, including hematologic or de novo lymphoid neoplasms. The total conquest of Hodgkin's disease seems to be an attainable objective; continued referrals to major cancer centers are important to ensure accurate diagnosis, proper staging, controlled trials, and identification of complications. (123 Refs)

MALIGNANT LYMPHOMA: DIAGNOSIS AND STAGING

16. USE OF IMMUNOGLOBULIN LIGHT CHAIN ANALYSIS TO DETECT BONE MARROW INVOLVEMENT IN B-CELL NEOPLASMS.

Sobol RE, Astarita RW, Chisari FV, Griffiths JC, Royston I
Dept. Medicine V-111E, Univ. California Sch. Medicine, La Jolla, CA, 92093
Clin Immunol Immunopathol; 24(1):139-144 1982

Double-blind analysis of bone marrow specimens from 15 patients with B-cell neoplasms and 10 controls was performed to determine whether immunoglobulin (Ig) light chain analysis (LCA) of bone marrow lymphoid cells is a more sensitive indicator of bone marrow involvement than light microscopic (LM) examination. Bone marrow aspirates were evaluated by a two-color immunofluorescence (IF) microscopic technique to determine the ratio of kappa-bearing lymphocytes to lambda-bearing lymphocytes (kappa/lambda ratio). Both bone marrow aspirate and biopsy specimens were reviewed by LM. Abnormal kappa/lambda ratios implied bone marrow involvement in 9/10 cases of non-Hodgkin's lymphoma (NHL), 4/4 cases of multiple myeloma (MM), and 1/1 case of Waldenstrom's macroglobulinemia (WM). All MM and WM cases had evidence for involvement by LM. Two NHL patients with abnormal kappa/lambda ratios had normal bone marrow morphology. LCA implied bone marrow involvement in 4/5 NHL patients with equivocal LM evaluations and in 3/3 cases with clear morphologic involvement. These data suggest that combined LCA and LM evaluation represent a more objective and inclusive method to detect bone marrow involvement in B-cell neoplasms than LM alone. (Author abstract) (14 Refs)

17. STUDIES OF TERMINAL DEOXYNUCLEOTIDYL TRANSFERASE IN NORMAL AND NEOPLASTIC HUMAN CELLS.

Campagnari F, Clerici L, Bombardieri E, Vezzoni P, Di Fronzo G, Villa ML, Buraggi GL
Lab. Biochemistry, Biology Group D.G. XII, C.E.C. Joint Res. Centre, 21020 Ispra (Va), Italy
Adv Exp Med Biol; 145:305-320 1982

Procedures for measurements of terminal deoxynucleotidyl transferase (TdT) activity and the immunofluorescence method for cells containing TdT were standardized and were used in analysis of 36 leukemia and 75 lymphoma patients not receiving chemotherapy. TdT was almost undetectable in the preparations from WBC of chronic lymphocytic leukemias and from 12 normal lymph nodes. The enzyme levels were well below the values of 10 units (U)/10(8) cells or 10 U/0.1 g lymphoid tissue, that were established as limits for discriminating between the trivial and the pathologically significant findings. Moreover, the cells from both sources did not fluoresce in the immunoassay for TdT. TdT was elevated in the neoplastic cells from 16/19 patients with acute lymphoblastic leukemia (ALL), and was practically undetectable only in 2 patients with common ALL and the single patient with B ALL. In the group of eight patients with common ALL whose blasts were analyzed biochemically and were found to contain appreciable amounts of enzyme, the concentration of TdT/10(8) cells ranged from 78-648 U with a mean value of 244 U. TdT was found in all 10 patients with lymphoblastic lymphoma, concentrations ranging from 289-1,301 U/0.1 g tissue with a mean of 630 U. In most malignant lymphoblasts the TdT immunofluorescence was restricted to the nuclei. Definite correlations between concentrations of enzymatic activity and percentage of immunofluorescent cells could not be established. (33 Refs)

18. THE PROGNOSTIC SIGNIFICANCE OF TERMINAL DEOXYNUCLEOTIDYL TRANSFERASE (TDT) IN PATIENTS WITH LEUKEMIAS AND MALIGNANT LYMPHOMAS.

Mertelsmann R
Developmental Hematopoiesis Lab., Dept. Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY, 10021
Adv Exp Med Biol; 145:259-277 1982

Activity of terminal deoxynucleotidyl transferase (TdT) was analyzed and the relationship to remission frequency and duration as well as survival in patients with acute lymphoblastic leukemia (ALL), acute nonlymphoblastic leukemia (ANLL), and malignant non-Hodgkin's lymphoma (NHL) in adults was investigated. All patients were diagnosed and treated according to standardized chemotherapy protocols. Of 113 patients treated on ALL protocols including 101 patients with ALL and 12 patients with lymphoblastic lymphoma, 44 patients were studied for TdT activity at diagnosis prior to treatment and an additional 38 patients after initiation of treatment or at relapse. Of 72 patients with evaluable TdT determinations, only 2 with B cell ALL and 1 with T cell ALL failed to exhibit elevated TdT activities. Pre-treatment bone marrow TdT activities were found to be significantly related to survival: patients exhibiting TdT activities less than 1 unit (U)/10(8) cells showed the longest survival. Thirteen of 91 patients with ANLL receiving chemotherapy exhibited elevated TdT activities as observed in ALL and 11 (12%) exhibited low (less than 0.1 U/10(8) cells) but unequivocal TdT activity. Of 52 patients with diffuse NHL treated with protocol chemotherapy, 50% of null cell lymphomas and 52% of T cell lymphomas exhibited high levels of TDT activity. These findings documented the prognostic significance regarding survival of levels of TDT activity in ALL, ANLL, and diffuse NHL. (32 Refs)

19. MORPHOMETRIC CHARACTERIZATION OF DIFFUSE LARGE-CELL (HISTIOCYTIC) LYMPHOMAS.

van der Valk P, Hermans J, Brand R, Cornelisse CJ, Spaander PJ, Meijer CJ
Pathologisch-Anatomisch Laboratorium, Univ. Medical Center, P.O. Box 9603, 2300 RC Leiden, The Netherlands
Am J Pathol; 107(3):327-335 1982

From 28 large-cell lymphomas, defined by marker studies, enzyme histochemistry, and electron microscopy as large noncleaved follicle center cell tumors (lnc FCC), B-immunoblastic or true histiocytic lymphomas, morphometric cell parameters, including nuclear size and shape, cytoplasmic area, and cytoplasm-to-nucleus ratio, were measured. Moreover, size, number, and location of nucleoli in the nuclei of the characteristic cells of lnc FCC and B-immunoblastic lymphoma were determined. Statistical evaluation of the data showed the nuclear shape to be the most sensitive parameter in the differentiation of true histiocytic lymphoma from lnc FCC and B-immunoblastic lymphomas. With nucleolar parameters lnc FCC could be differentiated from B-immunoblastic lymphoma: lnc FCC had a higher mean number of nucleoli per cross-section of nucleus and more eccentrically located nucleoli. Moreover, the measurements show that the differences in number and location of nucleoli between large noncleaved follicle center cells and B-immunoblasts are smaller than generally described in the literature. our results show that it is possible to differentiate by morphometry between lnc FCC, B-immunoblastic, and true histiocytic lymphomas. (Author abstract) (20 Refs)

20. CHILD'S NON-HODGKIN MALIGNANT LYMPHOMAS HISTOCYTOLOGY. STUDY OF 161 CASES APPLIED TO KIEL CLASSIFICATION.

Gerard-Marchant R, Bayle C, Caillou B
Laboratoire d'Histopathologie A, Institut Gustave-Roussy, F 94800 Villejuif, France
Ann Pathol; 2(2):107-116 1982

A retrospective study of the histology and the cytology of 161 children's (up to 15 yr of age) non-Hodgkin malignant lymphomas (ML) is presented, applying the Kiel classification. New sections were made from the paraffin embedded specimens, stained with various techniques, and the results of histology and cytology were discussed. Lymphoblastic ML represented 85% of the cases in this series. Lymphoblastic ML Burkitt-like type accounted for 59% of the lymphoblastic ML and 50% of all the cases in this series. The smears revealed middle-sized cells with dense nuclei bearing one or many small nucleoli. The cytoplasms were very basophilic and show small clear vacuoles. The 'starry sky pattern' had no diagnostic value. Lymphoblastic ML with convoluted nuclei represented 28% of the lymphoblastic ML and 25% of all the cases. Smears were not as helpful in diagnosis as sections which showed a loose pattern of cells with scanty cytoplasm and tridimensional convolutions of the largest nuclei. Unclassified lymphoblastic ML accounted for about 10% of the ML. The cells were similar to the preceding type but there were no convolutions of the nuclei. However, most of them also belonged to the T lymphoblastic ML. Immunoblastic ML is less frequent (10% of the cases) and were composed of large cells with conspicuous nuclei; the cytoplasm was more or less basophilic and often had PAS-positive inclusions. In nine cases (5.5%), a precise typing could not be achieved, however, all obviously belonged to the high grade ML. Good correlation between cell typing and anatomic localization was noted. Differential diagnosis is discussed. The Kiel classification was shown to be easy to apply and suitable for classifying childhood ML. (30 Refs) (In FRE)

21. PROGNOSIS OF LYMPHOSARCOMAS. MULTIVARIATE ANALYSIS IN A SERIES OF 334 PATIENTS.

Bonichon F, Durand M, Hoerni B, Lagarde C
Fondation Bergonie, 180, rue de Saint-Genes, F-33076 Bordeaux Cedex, France
Bull Cancer (Paris); 69(2):149-158 1982

In this retrospective study, we analyzed prognostic factors of 334 previously untreated patients with non Hodgkin's malignant lymphoma. the importance of the different prognostic variables was first studied with survival curves. Next, using a 'segmentation' method and a logistic regression analysis, we studied the factors influencing the complete remission rate which is the most important prognostic factor. For the 'low-grade' lymphosarcomas, with the segmentation method, we obtained five patient groups for which the complete remission rates varied between 7 and 95.5% according to clinical staging, age and mediastinal involvement. For the 'high-grade' lymphosarcomas, we obtained four patient groups in which the complete remission rates varied between 8.7 and 84.7% according to mediastinal and sub-diaphragmatic involvement and clinical staging. Lastly, the Cox model was used in order to determine the best variable combination capable of predicting the survival of patients with clinical Stages I or II. These variables were pathological grading, complete initial remission, clinical staging and BCG immunotherapy. With scores deduced from the Cox model, we were able to determine three prognostic groups for which the survivals at 3 yr were very significantly different (7 to 89%). (Author abstract) (18 Refs) (In FRE)

22. DIFFUSE LARGE CELL AND UNDIFFERENTIATED LYMPHOMAS WITH PROMINENT MEDIASTINAL INVOLVEMENT. A POOR PROGNOSTIC SUBSET OF PATIENTS WITH NON-HODGKIN'S LYMPHOMA.

Trump DL, Mann RB
Wisconsin Clinical Cancer Center, K4/662 CSC, 600 Highland Ave., Madison, WI, 53792
Cancer; 50(2):277-282 1982

This report describes 11 adults with non-Hodgkin's lymphoma who presented with symptoms caused by large mediastinal masses. Patients with lymphoblastic lymphoma were excluded from this analysis. Most of the patients were young women with localized disease at presentation. Ten tumors were diffuse large cell ('histiocytic') lymphomas and 1 was a diffuse, undifferentiated lymphoma, non-Burkitt's type. According to the Lukes' and Collins' classification scheme, seven were large cleaved cell type, three were large noncleaved and one was small noncleaved cell type. Sclerosis was present in four cases. Despite aggressive therapy nine patients died within 26 mo of diagnosis and only two remain disease-free. Median survival of these patients was 16 mo. Patients with symptomatic mediastinal masses and non-Hodgkin's lymphomas composed predominantly of large cell appear to share certain clinicopathologic features and to present a poor prognosis subset of patients with non-Hodgkin's lymphoma. (Author abstract) (28 Refs)

23. LYMPHOSCINTIGRAPHY BY SC INJECTION OF 67GA-CITRATE.

Ito Y, Otsuka N, Nagai K, Muranaka A, Yoneda M, Terashima H, Yanagimoto S
Div. Nuclear Medicine, Kawasaki Medical Sch., Kurashiki, Okayama-ken 701-01, Japan
Eur J Nucl Med; 7(6):260-265 1982

Lymphoscintigraphy with sc 67Ga-citrate (200 uCi) demonstrated lymph nodes effectively in 15 patients with lymph node metastasis or malignant lymphoma. Use of 67Ga-scintigraphy is recommended 5 min to 1 hr after sc injection of 67Ga. The positive results corresponded well to cold lesions detected by lymphoscintigraphy with 99mTc-rhenium colloid in metastatic lymph nodes. Possible mechanisms of localization are binding of 67Ga to transferrin in lymph and pinocytosis. A combination of colloid- and sc 67Ga-lymphoscintigraphy is suggested for diagnosis of lymph node disease. (9 Refs)

24. COMPUTED TOMOGRAPHY OF INTRACRANIAL LYMPHOMA.

Thomas M, Macpherson P
Dept. Neurology, Inst. Neurological Sciences, Southern General Hosp., Glasgow, Scotland
Clin Radiol; 33(3):331-336 1982

The appearances on computed tomography (CT) of 17 patients with histologically proven intracranial lymphoma have been analyzed and abnormalities detected in 16. Four of the patients had systemic lymphoma. Multiple lesions were seen in eight patients (47%), in six of whom the multiple lesions in each patient were of similar appearance. There was good macroscopic correlation between the CT and post-mortem appearances in the eight patients who subsequently died, although in five, histological examination showed more extensive infiltration. Meningeal involvement was seen more commonly in the cases of systemic lymphoma than in the purely cerebral lymphomas, but parenchymal lesions were equally common in both. Grey matter lesions tended to be clearly demarcated, of increased density with little edema or displacement; homogeneous density enhancement was produced by the intravenous injection of contrast medium. White matter lesions were usually poorly demarcated, of variable density with marked edema and displacement, and with heterogeneous enhancement. (Author abstract) (18 Refs)

25. MAMMOGRAPHY AND TELETHERMOGRAPHY IN THE DIAGNOSIS OF BREAST LYMPHOMA (28 CASES).

Vignanotti G, Bergonzi S, Guzzon A, Coopmans De Yoldi G, Farina F
Servizio di Radiologia, Istituto Nazionale Tumori, Milan, Italy
Radiol Med (Torino); 68(6):455-462 1982

Mammography and telethermography were used to evaluate 28 patients with breast lymphoma. Signs of primary malignancy were revealed by the mammography in 10/15 patients; in 6/10 there was focal neoplasia of an epithelial type, and in 4/10 there was carcinomatous mastitis. In secondary malignancies, the mammography revealed signs of malignancy in 6/11 patients, with carcinomatous-like lesions in two of the patients and carcinomatous mastitis in four. Three patients with Hodgkin's lymphoma presented mammographic findings suggestive of inflammatory disease. The telethermography was carried out in 15/28 patients; in 13/15 it was significantly useful in localizing primary tumors when the hyperthermia was equal to or higher than 2 C. This procedure was particularly useful in two cases of Hodgkin's disease, with hyperthermias of 2 C and 5 C. The mammography gave positive results for malignancy in 18/28 cases (65%); mammography combined with telethermography led to accurate diagnoses of malignancy in 23/28 cases (82%). Due to variation in the radiological patterns, exact diagnoses were often uncertain, and no significant difference between primary or metastatic disease could be seen in radiological patterns of non-Hodgkin lymphomas. (14 Refs) (In ITA)

26. PRIMARY LYMPHOMA OF BONE: RELATIONSHIP OF RADIOGRAPHIC APPEARANCE AND PROGNOSIS.

Phillips WC, Kattapuram SV, Doseretz DE, Raymond AK, Schiller AL, Murphy G, Wyshak G
Dept. Radiology, Massachusetts General Hosp., Boston, MA, 02114
Radiology; 144(2):285-290 1982

A retrospective review was made of the pretreatment radiographs of 20 patients with well-documented primary lymphoma of bone. Nine radiographic signs were defined, and the presence or absence of each was recorded for each patient. When the radiographic findings were compared with disease-free survival for each patient, it was found that patients who had a relapse had a higher mean number of positive radiographic signs than those who remained disease free (p less than 0.02). Also, those who relapsed early had more positive signs than those who relapsed late (p less than 0.05). Certain signs, ie, pathologic fracture, layered periosteal new bone, broken periosteal new bone, cortical breakthrough, soft-tissue mass, and soft-tissue swelling, were more helpful than others for making a prognosis. These signs appear to be related to radiologic evidence of imminent or actual soft-tissue extension of the tumor. (Author abstract) (14 Refs)

27. HYPOPIGMENTED MYCOSIS FUNGOIDES: REPORT OF FIVE CASES WITH ULTRASTRUCTURAL OBSERVATIONS.

Breathnach SM, McKee PH, Smith NP
(c/o Smith) Skin Tumour Unit, St. John's Hosp., Lisle St., London WC2H 7BJ, England
Br J Dermatol; 106(6):643-649 1982

Five dark-skinned individuals presented with widespread well-demarcated hypopigmented lesions, biopsy of which revealed the histopathological features of mycosis fungoides. Ultrastructural studies showed focal invasion of the epidermis by mycosis cells with degenerative changes in adjacent melanocytes and keratinocytes. The majority of melanocytes exhibited swelling of cytoplasmic organelles and disordered melanogenesis with production of spherical incompletely melanized melanosomes. In addition disintegrating melanocytes were occasionally seen. Perifollicular repigmentation within hypopigmented areas occurred in two patients following clearing of the epidermal infiltrate with PUVA therapy. Mycosis fungoides may present with areas of cutaneous hypopigmentation. (Author abstract) (17 Refs)

28. SKELETAL MANIFESTATIONS IN CUTANEOUS T-CELL LYMPHOMAS.

Brigham BA, Bunn PA, Horton JE, Schechter GP, Wahl LM, Bradley EC, Dunnick NR, Matthews MJ
(c/o Bunn) Navy Medical Oncology Branch, NCI, Natl. Naval Medical Center, Bethesda, MD, 20814
Arch Dermatol; 118(7):461-467 1982

The clinical course of three patients with cutaneous T-cell lymphoma (CTCL) in whom skeletal disease developed is presented and the literature on skeletal involvement in these disorders is reviewed. Three separate types of skeletal manifestations occurred: (1) osteolytic lesions, (2) osteoblastic lesions, and (3) diffuse osteoporosis. Hypercalcemia was present in two cases. Tumor cells from two patients in short-term culture secreted osteoclast-activating factor(s). Both of these patients had pathologic evidence of osteoclast activation in bone sections. Thus, the tumor cells in certain patients with CTCL may derive from a monoclonal proliferation of a T-cell subset capable of producing humoral bone-resorbing factor(s) similar to those demonstrated in cultures of mitogen- and antigen-activated normal lymphocytes. Since skeletal lesions are unusual, it would follow that other T-cell subsets account for pathologic cell proliferation in most patients with CTCL. (Author abstract) (45 Refs)

29. VISUALIZATION OF SKELETAL MUSCLE INVOLVEMENT OF MYCOSIS FUNGOIDES ON 67GA SCINTIGRAPHY.

Shigeno C, Morita R, Fukunaga M, Tsuchiya K, Hino M, Harioka T, Torizuka K
Dept. Nuclear Medicine, Kytoto Univ. Sch. Medicine, 54 Shogoin-kawara-machi, Kyoto 606, Japan
Eur J Nucl Med; 7(7):333-335 1982

An uncommon involvement of the skeletal muscle by mycosis fungoides detected by 67Ga-citrate scintigraphy in a 84-yr-old female is described. The patient developed generalized erythema 17 yr prior to the admission. The patient was successfully treated with corticosteroids and regional radiotherapy. For the following 15 yr the patient's condition had remained good until 2 mo prior to the admission. Diagnosis of mycosis fungoides was made by skin biopsy. The patient was treated with systemic chemotherapy and with regional radiotherapy. The patient's condition progressively deteriorated. The patient died of bronchopneumonia approx 6 wk after 67Ga scanning. Autopsy section from the left leg showed diffuse infiltration of malignant lymphomatous cells in all soft tissue components from the skin to the underlying calf muscle. (11 Refs)

MALIGNANT LYMPHOMA: CLINICAL IMMUNOLOGY AND IMMUNOTHERAPY

30. ABNORMAL IMMUNOREGULATION IN PATIENTS WITH NON-HODGKIN'S MALIGNANT LYMPHOMAS. I. INCREASED HELPER FUNCTION OF PERIPHERAL BLOOD T LYMPHOCYTES.

Gajl-Peczalska KJ, Chartrand SL, Bloomfield CD
Dept. Lab. Medicine and Pathology, Univ. Minnesota, Minneapolis, MN, 55455
Clin Immunol Immunopathol; 23(2):366-378 1982

T lymphocytes isolated from the blood of 24 newly diagnosed and 2 relapsed patients with non-Hodgkin's malignant lymphomas were studied for helper/suppressor activity in cocultures with allogeneic tonsillar B lymphocytes stimulated with pokeweed mitogen. The IgA, IgG, and IgM secretion was measured by double-antibody radioimmunoassay. In 85% of patients with B lymphomas their T lymphocytes produced a severalfold increase in immunoglobulin secretion when compared with age-matched healthy controls. By contrast in two cases of T lymphoma, suppression of immunoglobulin secretion was observed. The ratio of 'T helper'/'T suppressor' lymphocytes, as measured with monoclonal antibodies (OKT4/OKT8), were similar for patients and controls, and concanavalin A-induced suppression was equally good. However, small numbers of patient T lymphocytes provided good help, while control cells failed in these higher dilutions. Possible explanations of the increased helper activity of 'nonmalignant' T lymphocytes in B lymphomas as related to clinical features and the pathogenesis of B- versus T-cell malignancies are discussed. (Author abstract) (31 Refs)

31. T-LYMPHOCYTE SUBSETS IN FOLLICULAR LYMPHOMAS COMPARED WITH THOSE IN NON-NEOPLASTIC LYMPH NODES AND TONSILS.

Dvoretsky P, Wood GS, Levy R, Warnke RA
Dept. Pathology, Rochester General Hosp., 1425 Portland Ave., Rochester, NY, 14621
Hum Pathol; 13(7):618-625 1982

Using monoclonal antibodies on frozen sections, the authors define the anatomic localization of T-lymphocyte subsets in follicular lymphomas as well as in nonneoplastic lymph nodes and tonsils. The percentage of Leu-1+ T cells in the follicles of follicular lymphomas (20%) was virtually identical to that seen in the follicles of nonneoplastic lymph nodes or tonsils (22%). There were 50% T cells in the interfollicular regions of follicular lymphomas and 75% in the paracortical regions of the nonneoplastic specimens. In neoplastic follicles the number of Leu-3a+ cells was 67% of the number of Leu-1+ cells, whereas virtually the entire T-cell population in the nonneoplastic follicles expressed the Leu-3a antigen. These T cells of helper phenotype may facilitate the neoplastic process or an immune response against it or may be bystanders to the B-cell proliferation. (Author abstract) (22 Refs)

32. PHENOTYPE OF CELLS INVOLVED IN MYCOSIS FUNGOIDES AND SEZARY SYNDROME (BLOOD AND SKIN LESIONS): IMMUNOMORPHOLOGICAL STUDY WITH MONOCLONAL ANTIBODIES.

Schmitt D, Souteyrand P, Brochier J, Czarnielewski J, Thivolet J
Dept. Dermatology, Hopital Edouard-Herriot, F-69374 Lyon Cedex 2, France
Acta Derm Venereol (Stockh); 62(3):193-199 1982

The phenotypic expression of immunocompetent cells involved in lesions of cutaneous T-cell lymphoma (mycosis fungoides and Sezary syndrome) was studied by using monoclonal antibodies specific for T-cell subsets and HLA-DR antigens (OKT3, T4, T6, T8) (BL 6, BL 5, BL 2). In Sezary syndrome, the phenotype of Sezary cell is homogeneous (T3+, T4+, T8-, T6-, BL2-) and corresponds to the phenotype expressed by the normal helper T-cell population. At the ultrastructural level, the discontinuous distribution of OKT4 and OKT3 antigenic sites on the cell surface is similar to the HTLA antigens. In skin lesions, the Langerhans cells expressed two specificities shared by normal thymocytes (T6 and BL6). We suggest that the expression of these antigens could be related to the epithelial microenvironment (epithelium-dependent differentiation antigens). The tumoral lymphoid cells infiltrating the skin showed the same phenotype (helper type) as the circulating Sezary cells (T3+, T4+, T8-, T6-). Moreover, The T3+ cells also expressed HLA-DR antigens and corresponded to activated T lymphocytes. The various subpopulations of immunocompetent cells seemed to be related to the MHC-derived antigens. (Author abstract) (29 Refs)

MALIGNANT LYMPHOMA: CHEMOTHERAPY

33. RANDOMIZED STUDY COMPARING DOXORUBICIN, CYCLOPHOSPHAMIDE, VINCRISTINE, METHOTREXATE WITH LEUCOVORIN RESCUE, AND CYTARABINE (ACOMLA) WITH CYCLOPHOSPHAMIDE, DOXORUBICIN, VINCRISTINE, PREDNISONE, AND BLEOMYCIN (CHOP-B) IN THE TREATMENT OF DIFFUSE HISTIOCYTIC LYMPHOMA.

Newcomer LN, Cadman EC, Nerenberg MI, Chen M, Bertino JR, Farber LR, Prosnitz LR
Dept. Internal Medicine, Section Medical Oncology, Yale Univ. Sch. Medicine, 333 Cedar St., P. O. Box 3333, New Haven, CT, 06510
Cancer Treat Rep; 66(6):1279-1284 1982

Two combination chemotherapy programs. ACOMLA (doxorubicin, cyclophosphamide, vincristine, methotrexate with leucovorin rescue, and cytarabine) and CHOP-B (cyclophosphamide, doxorubicin, vincristine, prednisone, and bleomycin), were evaluated in 29 prospective randomized patients with advanced diffuse histiocytic lymphoma. A complete response was achieved in 13 of the 15 patients (87%) treated with CHOP-B and in 9 of the 14 patients (64%) treated with ACOMLA. The overall complete response rate was 75%. Two patients treated with ACOMLA and none of the CHOP-B-treated patients have relapsed. Median followup is 32 months for ACOMLA patients and 26 months for CHOP-B patients. Actuarial freedom from relapse at 2 years is 49.9% for ACOMLA and 93.3% for CHOP-B (p = 0.01). Toxicity was substantial, with eight nonfatal episodes of sepsis and three drug-related deaths. There have been no central nervous system relapses. Although patients treated with CHOP-B have a better response rate, the small numbers of patients treated to date preclude definitive conclusions. (Author abstract) (16 Refs)

34. COMBINATION CHEMOTHERAPY IN ADVANCED MALIGNANT LYMPHOMA WITH BLEOMYCIN, VINCRISTINE, ADRIAMYCIN AND PREDNISOLONE (BOAP).

Kurita S, Kamei Y, Murakami M, OyamaA, Goto T, Fukushima M, Ota K
Second Dept. Internal Medicine, Aichi Cancer Center, Aichi, Japan
Rinsho Ketsueki; 23(1):61-67 1982

Bleomycin (15 mg/wk, im), vincristine (1 mg/wk, iv), adriamycin (60 mg every 3 wk, iv), and prednisolone (60-30 mg/day every day x 2 wk) were administered in combination as the BOAP chemotherapeutic regimen to 23 patients (14 men, 9 women; 14-64 yr old) with malignant lymphoma. The lymphomas included nine reticulosarcomas, two lymphosarcomas, four giant filter cell lymphomas, and six cases of Hodgkin's disease. Complete remission was observed in 13/23 patients; 10/13 were patients undergoing therapy for the first time. Complete remission was observed in 9/12 non-Hodgkin's lymphoma patients undergoing therapy for the first time. According to the type of non-Hodgkin's lymphoma, complete remission was observed in 3/5 with T cell type lymphoma and in 6/10 with B cell type lymphoma. Complete remission was also observed in 3/8 patients who had received prior treatment. Hair loss, leukocytopenia (4,000-2,000 WBC), and peripheral neuropathy were the primary side effects of the therapy. Fever, obstruction of the lungs, thrombocytopenia, and gastrointestinal symptoms were also observed. Seventy percent of the patients who achieved complete remission survived greater than 2 yr after diagnosis. (16 Refs) (In JPN)

35. COMBINATION CHEMOTHERAPY OF ADVANCED NON-HODGKIN'S LYMPHOMA WITH ADRIAMYCIN, VINCRISTINE, IFOSFAMIDE AND PREDNISOLONE (AVIP): A PRELIMINARY REPORT.

Ohnoshi T, Oka A, Hayashi K, Ueoka H, Sato M, Nishihara R, Yasuoka M, Sando Y, Tanaka T, Kimura I

Second Dept. Medicine, Okayama Univ. Hosp., Okayama 700, Japan

Acta Med Okayama; 36(1):67-72 1982

Eighteen patients with advanced non-Hodgkin's lymphoma other than the diffuse histiocytic type were treated with a combination of adriamycin, vincristine, ifosfamide and prednisolone (AVIP). The objective response rate was 83% (15/18); 61% (11/18) achieved complete remission. The median duration of complete remission was 11 mo ranging from 2 to 39+ mo. Eleven of the 18 patients are still alive during the median follow-up time of 13 mo. The median survival was 14+ mo for complete responders, and 9.5 mo for partial and nonresponders. A myelosuppressive toxicity was well tolerated. AVIP offers some hope as treatment of advanced non-Hodgkin's lymphoma. (Author abstract) (14 Refs)

36. THE TREATMENT OF DISSEMINATED NON-HODGKIN'S LYMPHOMA OF UNFAVORABLE HISTOLOGY.

Gallagher CJ, Copplestone A, Meikle JD, Lister TA

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Cancer Chemother Pharmacol; 8(2):237-241 1982

Long-term follow-up of 48 patients with advanced non-Hodgkin's lymphoma of unfavorable histological type is reported. Complete remission (CR) was achieved in 24/48 patients with primary induction therapy (adriamycin, vincristine, prednisolone and L-asparaginase). Those under 55 yr old had significantly higher response, 20/32 compared to 4/16. CR rate was higher for those with nodal than for those with extranodal disease. For patients with Stage IV disease the only extranodal site associated with a significantly worse prognosis was the CNS, CR being achieved in 1/9 patients compared to 10/22 for all other sites. Twenty-three of 24 patients who did not achieve CR have died. Resistant lymphoma, despite an adequate trial of therapy was encountered in 17 patients. Of these, 10 received alternative therapy; three responded and one achieved a prolonged CR. Nine of 24 patients remain in CR 3-7 yr after entering it. The remaining 15 have relapsed, 14 within 18 mo and 1 at 4 y. Twenty-one patients received full CNS prophylaxis after CR was achieved. Three had CNS relapse, as did one of the complete remitters who did not receive prophylaxis. Twelve patients were alive and free of disease between 3 1/2 and 8 1/2 yr, nine in first remission, two have relapsed but currently free of disease, and one had failed primary induction therapy but subsequently remitted. (12 Refs)

MALIGNANT LYMPHOMA: SURGERY

37. THE ROLE OF SURGERY IN THE MANAGEMENT OF AMERICAN BURKITT'S LYMPHOMA AND ITS TREATMENT.

Kemeny MM, Magrath IT, Brennan MF
Dept. Surgery, City of Hope Natl. Medical Center, 1500 East Duarte Road, Duarte, CA, 91010
Ann Surg; 196(1):82-86 1982

Ninety-two patients with American Burkitt's lymphoma were studied retrospectively to elucidate the role of surgery in the complications of treatment of Burkitt's lymphoma. All of the patients reviewed had been treated with a least one chemotherapeutic agent. Seventy-five percent of the patients had predominantly abdominal disease that required a laparotomy for diagnosis and treatment when possible. The postoperative complications, such as infections, were not more frequent when compared with other elective surgical procedures. Ten percent of all the patients had episodes of significant gastrointestinal bleeding secondary to disease or to the chemotherapy. One patient was treated surgically, and two patients had fatal hemorrhages. Further abdominal complications that required surgery included intussusception, cholelithiasis, small bowel obstruction, and bowel perforation. The incidence of renal failure because of electrolyte imbalance from tumor lysis syndrome was 30%. One third of these patients required access for dialysis. Ten percent of patients developed hemorrhagic cystitis, but none required surgery. Surgery was necessary in five patients with life-threatening pericardial effusion. Other surgical treatments are also reviewed. It is concluded that Burkitt's lymphoma has a significant cure rate with the appropriate medical and surgical therapies, and that the surgical approach to the disease and its complications should be optimistic and appropriately aggressive. (Author abstract) (14 Refs)

MALIGNANT LYMPHOMA: CASE REPORTS

38. THE TREATMENT OF LYMPHOBLASTIC LYMPHOMA WITH ANTITHYMOCYTE GLOBULIN.

Wong KK, Sweet DL, Variakojis D
(c/o Sweet) Dept. Medicine, Univ. Chicago Hosp. and Clinics, Box 420, 950 East 59th St., Chicago, IL, 60637
Cancer; 50(1):57-61 1982

A 20-yr-old man with previously treated lymphoblastic lymphoma, a known T-cell disorder, developed progressive disease despite intensive combination chemotherapy with doxorubicin, vincristine, and prednisone. He was subsequently treated with a 21-day course of iv antithymocyte globulin at a dose of approx 15 mg/kg per day. This resulted in a marked reduction in lymphadenopathy as determined by physical examination and chest x-ray. Toxicity was limited to minor pruritis which resolved with diphenyldramine and hydrocortisone premedication. (Author abstract) (26 Refs)

39. PRIMARY LYMPHOMA OF THE SPINAL CORD.

Slager UT, Kaufman RL, Cohen KL, Tuddenham WJ
Dept. Pathology, Rancho Los Amigos Hosp., 7705 Golondrinas Ave., Downey, CA, 90242
J Neuropathol Exp Neurol; 41(4):437-445 1982

Lymphomas may occur in the central nervous system either as primary lesions or secondary to lymphomas in other sites. While lymphomas secondary to generalized lymphoproliferation may occur in either the brain or the spinal cord, primary lymphomas are found almost exclusively in the brain. Only three primary lymphomas of the cord have been reported. We recently had the opportunity to study a fourth case. Spinal cord lymphoma was not the diagnosis considered in any of these cases. Since the lesion is radiosensitive, inclusion of primary lymphoma in the differential diagnosis of obscure spinal cord tumors could result in a histological diagnosis and effective therapy. (Author abstract) (12 Refs)

40. TREATMENT OF CUTANEOUS T-CELL LYMPHOMA WITH A NEW AROMATIC RETINOID (RO 10-9359).

Claudy AL, Delomier Y, Hermier C
Dept. Dermatology, Hopital Bellevue, F-42000 St. Etienne, France
Arch Dermatol Res; 273(1/2):37-42 1982

Low-grade malignant lymphoma of the skin in a 77-yr-old woman, who presented with a 3-mo history of rapidly growing nodular lesions on the trunk and limbs, was treated with Ro 10-9359 (1.0 mg/kg/day) as maintenance therapy. Mild cheilitis was produced by Ro 10-9359 therapy. After 34 days of treatment, all the lesions became macular and pigmented, and no new lesions occurred. Discontinuation of chemotherapy resulted in relapse. (21 Refs)

MALIGNANT LYMPHOMA: SELECTED REPORTS ON ETIOLOGY AND EPIDEMIOLOGY

41. LYMPHOMA RISK IN COELIAC DISEASE OF LATER LIFE.

Cooper BT, Holmes GK, Cooke WT
Univ. Dept. Medicine, Bristol Royal Infirmary, Bristol BS2 8HW, England
Digestion; 23(2):89-92 1982

From 314 patients with celiac disease, 20 patients were found to have developed a lymphoma. The incidence of lymphoma was much greater in the 6th, 7th and 8th decades of life than in the previous 2 decades. In 12 patients, the lymphoma was diagnosed within 4 yr of the diagnosis of their coeliac disease and there were significantly more of these lymphomas appearing in celiac diagnosis between 51 and 80 yr, who made up 23% of the series, than in those diagnosed between 21 and 50 yr. We conclude that lymphoma is particularly a complication of older celiacs and that celiacs newly diagnosed at more than 50 yr of age should be more closely followed up for they have a 1 in 10 chance of harboring a lymphoma. (Author abstract) (12 Refs)

MALIGNANT LYMPHOMA: SELECTED PRE-CLINICAL STUDIES

42. HOMOGENEOUS POPULATIONS OF MACROPHAGES FROM HISTIOCYTIC LYMPHOMA PATIENTS AS A SOURCE OF MACROPHAGE SUBPOPULATIONS WHICH DIFFER IN IMMUNOREGULATORY PROPERTIES.

Lavie G, Shoenfeld Y, Shaklai M, Aderka D, Pick AI, Pinkhas J
(c/o Shoenfeld) Dept. Internal Medicine D, Beilinson Medical Center, Petach Tigra, H 9100, Israel
Cancer; 50(1):69-77 1982

The existence of subpopulations of macrophages which express a variety of regulatory activities of other branches of the immune system is suggested in a comparative study of a human macrophage long term culture ZI and a macrophage cell line DAB-1. Both cell cultures were derived from pleural effusions of patients with diffuse histiocytic lymphoma. DAB-1 cells were found to secrete factors which strongly suppress the response of normal T and B lymphocytes to the mitogens PHA, Con-A and pokeweed mitogen (PWM) (by 96-98%) and to stimulate the cytotoxic activity of NK cells. ZI cells secrete factors which have a mild inhibitory effect on the response of lymphocytes to the T-cell mitogens PHA and Con-A and a stimulatory effect on the response to PWM, whereas very little effect could be detected on the activity of NK cells. While DAB-1 cells form large clusters during growth in culture, and are capable of inducing the formation of lymphocyte rosettes around the tumor cells, ZI cells grow as a homogeneous monolayer and could not be shown to form such rosettes. The differences in the behavior of the two cell populations suggest that the malignant transformation may have affected different subsets of macrophages in each case. Cells from histiocytic lymphoma patients may therefore be a source for homogeneous subpopulations of macrophages and their isolation and propagation in culture is one approach by which such subsets can be defined characterized and classified. The biological characterization of macrophage subsets may also be of clinical importance since a transformed subset with broad suppressor activities may lead to a violent and rapidly deteriorating course of disease, as was in the case of the patient from whom the DAB-1 cell line was derived. (Author abstract) (31 Refs)

MALIGNANT LYMPHOMA: REVIEWS

43. BURKITT'S LYMPHOMA.

Ziegler JL
Veterans Admin. Medical Center, San Francisco, CA
CA; 32(3):144-161 1982

Etiology, clinical features, staging, treatment, and immunology of Burkitt's lymphoma are reviewed. Most, but not all cases are associated with Epstein-Barr virus (EBV); the causative role of EBV, if it exists, may be related to differences in viral strains. In addition to EBV, genetic factors, immunoregulatory determinants related to environment, and possibly an RNA virus have also been suggested as causes. Systemic chemotherapy is the treatment of choice. After complete remissions lasting about 1 yr, recurrence is rare. Prognosis is directly related to the tumor burden upon initial presentation. Burkitt's lymphoma is one of a dozen neoplasms that can be cured by drugs alone. It is the most likely candidate for a virus-induced human tumor. Studies of the association of Burkitt's lymphoma and EBV led to the discovery of EBV as the cause of infectious mononucleosis. Experimental and clinical studies of Burkitt's lymphoma have led to important advances in immunobiology and tumor immunology. Promising approaches in immunotherapy include rapid removal of antigen excess and immune complexes from the circulation and enhancement of normal immunoregulatory controls of the body. (121 Refs)

44. MALIGNANT LYMPHOMA OF THE SKIN: A REVIEW OF RECENT ADVANCES IN DIAGNOSIS AND CLASSIFICATION.

Holbert JM, Chesney TM

Dept. Pathology, Baptist Memorial Hosp., 899 Madison Ave. Room 502-A, Memphis, TN, 38146

J Cutan Pathol; 9(3):133-168 1982

In this review we have summarized the literature on malignant lymphomas involving the skin as well as on the histopathologic features which define benign cutaneous lymphoid infiltrates. In a diagnostically difficult case, the histopathologic features which include the following: B cell malignant lymphoma of the skin usually has a massive diffuse dermal infiltrate with a tendency to predominantly involve the lower reticular dermis and subcutis, with variable sparing of the papillary dermis. The infiltrate is usually separate from the overlying epidermis, which is frequently normal, and spreads through the adjacent dermis with infiltrating margins. The cellular infiltrate is usually monomorphous but will, in the case of mixed cell lymphomas, have an admixture of large and small atypical lymphoid cells. There is often infiltration by the cellular infiltrate into dermal appendages and walls of vessels and into subcutaneous fat. Conspicuous by their absence are eosinophils, plasma cells, and lymphoid germinal centers. Histologic features opposite to those outlined above are seen in benign lymphocytic infiltrates of the skin. If the skin biopsy of cutaneous lymphoma is of adequate size and handled very carefully by both the clinician performing the biopsy and the laboratory processing it, then the diagnostic criteria for classification of lymphoma in lymph nodes can be applied to the skin. This latter feature becomes important as our knowledge of the natural history and therapeutic response of different subtypes of malignant lymphoma can involve the skin and may initially present in the skin, although the eponymic lymphomas, Hodgkin's disease and Burkitt's lymphoma, appear to present in this manner quite infrequently. The least satisfactory histopathologic aspect of cutaneous lymphoma in 1982 is our inability confidently to diagnose the early stages of cutaneous T-cell lymphomas. (Author abstract) (61 Refs)

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HODGKIN'S DISEASE: DIAGNOSIS AND STAGING

1. VALUE OF SUBSTAGING MEDIASTINAL HODGKIN'S DISEASE (MHD) INTO PERICARDIAL (EP) AND CHEST WALL INVASION (EC) SUBSETS (MEETING ABSTRACT).

Rostock RA, Siegelman SS, Lenhard R, Wharam MD, Order SE
Department of Radiation Oncology, The Johns Hopkins Hospital, Baltimore, MD
Twenty-fourth Annual Meeting of the American Society of Therapeutic Radiologists, October 25-29, 1982, Orlando, Florida American Society of Therapeutic Radiologists; 1982

Thirty-five patients presenting with Hodgkin's Disease had thoracic CT scanning that resulted in an alteration in the known distribution of disease in 16/35 patients and 11/35 modifications in the treatment port and treatment philosophy which was not appreciated by upright PA and lateral chest x-rays. Sites of involvement included 23 anterior mediastinal, 15 peritracheal, 10 pericardial or paracardiac, 7 hilar, 5 chest wall invasion, 4 aortic arch, 3 lung, 3 sternum, and 1 retrocardiac disease. Ep and Ec invasion were more common than reported in the literature and appreciation of the full extent of the disease resulted in major changes in treatment ports and philosophy. All cases of Ec and Ep were nodular sclerosing histology and had associated anterior and/or peritracheal lymphadenopathy. Twelve out of 14 Ec and Ep had M/T ratios on upright chest x-ray (mass dimension divided by the widest thoracic cage diameter) of greater than .30 and 12/20 MHD cases with M/T ratios greater than .30 hd Ec or Ep involvement. These results may account for one of the reasons for the high reported failure rate of bulky MHD treated with radiation therapy alone. Patients with M/T greater than .30 have an intrathoracic control rate of 95% in this study, with combination radiation plus chemotherapy reserved for only advanced stage disease or extensive Ec or Ep. The use of CT scanning in all patients and substaging MDH into Ec and Ep subsets will allow more accurate treatment assessment and evaluation of treatment programs, and possibly reduction in risk/benefit ratios. (no Refs)

2. ASSESSMENT OF BONE MARROW HISTOLOGY IN HODGKIN'S DISEASE: CORRELATION WITH CLINICAL FACTORS.

Bartl R, Frisch B, Burkhardt R, Huhn D, Pappenberger R
Abt. Knochenmarksdiagnostik, Medizin. Klinik Innenstadt, Ziemssenstr. 1a, D-8000 Munchen 2, W. Germany
Br J Haematol; 51(3):345-360 1982

Bone marrow biopsies of 491 untreated and 170 treated patients with Hodgkin's disease (HD) were investigated. Marrow involvement was found in 10% and 25% respectively. Positive biopsies were rare in clinical Stages I and II (1% and 2%), but the incidence rose to 25% and 45% in Stages III and IV. HD patients with nodular sclerosis in lymph node histology had a low incidence of bone marrow involvement (4%), while those with lymphocytic depletion had a high incidence (22%). Of nine clinical and six histological parameters tested, bone marrow involvement proved to be the most significant predictive factor indicating an unfavorable course. Moreover, classification of the bone marrow manifestations according to the degree of lymphocytic infiltration, proved to be simple, reproducible and prognostically significant. Normal hematopoietic tissue was found in only 20% of the negative biopsies of untreated patients. The remaining 80% were characterized by a variety of non-specific reactions. These included marrow hypoplasia and leukemoid and exudative reactions each of which indicated a poor prognosis; and epithelioid-cell granulomas and lymphoid nodules which predicted favorable survival curves. Adequate bone marrow biopsy is a valuable part of the investigation of patients with HD, as both positive and negative biopsies provide information of prognostic significance. (Author abstract) (49 Refs)

3. AN EVALUATION OF THE NECESSITY FOR STAGING LAPAROTOMIES IN CLINICAL STAGES IA AND IIA HODGKIN'S DISEASE (MEETING ABSTRACT).

Taylor E, Griffin T, Lock M, Hafermann M, Kurtz J

Department of Radiation Oncology, University of Washington Hospital, Seattle, WA, 98195

Twenty-fourth Annual Meeting of the American Society of Therapeutic Radiologists, October 25-29, 1982, Orlando, Florida American Society of Therapeutic Radiologists; 1982

One hundred fourteen patients with Clinical Stages IA or IIA supradiaphragmatic Hodgkin's Disease were seen between 1968 and 1981. All patients were initially treated with extended field radiation therapy only (mantle plus paraaortic/splenic). Forty-one patients had staging laparotomies and 73 did not. Nine of the 41 laparotomy-staged patients turned out to be pathological Stage IIIA (22%). The actuarial 5-year survival rates were 94% for the laparotomy-staged group and 91% for the clinically-staged group. The pelvic recurrence rates were 2/41 (5%) and 5/73 (7%) respectively. The 5-year relapse-free survival rates were 81% for the laparotomy-staged group and 73% for the clinically-staged group. There are no statistically significant differences between the two groups of patients in terms of actuarial survival, disease-free survival, and pelvic recurrence rates. (no Refs)

4. PULMONARY INVOLVEMENT IN HODGKIN'S DISEASE. STUDY OF 49 CASES. II. DIAGNOSIS. DIFFERENTIAL DIAGNOSIS. ASSOCIATION WITH OTHER DISEASES.

Puras Tellaeche A, Frieyro Segui JE

Clinica Puerta de Hierro, Universidad Autonoma, Madrid, Spain

Rev Clin Esp; 164(5):285-291 1982

The diagnosis and differential diagnosis of pulmonary involvement in 49 patients with Hodgkin's disease is described. Radiology was found to be the most valuable diagnostic methods. Parenchymal involvement may be subpleural, interstitial and intrabronchial. Pleural involvement appeared as pleural effusion. Cytology was found to be of very low diagnostic value. Pulmonary infections, lung cancer, metastases and sarcoidosis should considered in differential diagnosis. (67 Refs) (In SPA)

HODGKIN'S DISEASE: CLINICAL IMMUNOLOGY AND IMMUNOTHERAPY

5. THE IN VIVO EFFECT OF A THYMIC FACTOR (THYMOSTIMULIN) ON IMMUNOLOGIC PARAMETERS OF PATIENTS WITH UNTREATED HODGKIN'S DISEASE.

Martelli MF, Velardi A, Rambotti P, Cernetti C, Bertotto A, Spinozzi F, Bracaglia AM, Falini B, Davis S
(c/o Davis) Dept. Oncology/Hematology, Veterans Admin. Medical Center, East Orange, NJ, 07019

Cancer; 50(3):490-497 1982

The in vivo effect of a calf thymus extract (thymostimulin, TS) on the E-rosetting capacity, PHA blastogenic response, serum migration inhibitory activity (LIF) and skin reactivity to recall antigens was evaluated in 19 untreated patients with Hodgkin's disease. In patients the mean percentage of peripheral blood lymphocytes forming E-rosettes increased from 47 to 55.7% (p less than or equal to 0.001; normal: 58.9). The mean PHA stimulation index rose with all three concentrations tested but did not reach normal values. Serum LIF was positive in only one patient prior to treatment with a total patient mean LIF of 1.03. Nine patients developed a positive LIF following treatment with a mean LIF for all patients of 0.75 (p less than or equal to 0.005). Skin tests were positive in 10 patients (52.6%) prior to therapy and 18 patients following therapy (94.7%; p less than or equal to 0.05). Thymostimulin, in vivo, appears to return immunologic competency to a population of untreated patients with Hodgkin's disease. (Author abstract) (74 Refs)

HODGKIN'S DISEASE: RADIOTHERAPY

6. A STUDY OF THE IMMUNOLOGIC EFFECTS OF LYMPHOID IRRADIATION IN HUMAN AND NON-HUMAN PRIMATES: CELLULAR CHANGES AND THE POTENTIAL FOR TRANSPLANTATION (MEETING ABSTRACT).

Halperin EC, Haas GS, Dosoretz DE, Gitterman MS, Cosimi AB, Linggood RM, Suit HD
Department of Radiation Medicine, Massachusetts General Hospital, Boston, MA, 02114

Twenty-fourth Annual Meeting of the American Society of Therapeutic Radiologists, October 25-29, 1982, Orlando, Florida American Society of Therapeutic Radiologists; 1982

Lymphoid irradiation (LI) is a powerful immunosuppression agent causing prolonged allograft survival and antigen specific tolerance in many experimental models. Previous reports have suggested that the immunosuppressive effect of LI are related to changes in the T cell peripheral blood levels (T-PBL). We prospectively studied 13 patients with stages I and II Hodgkin's Disease before, during, and after a course of LI. Forty-45Gy delivered to the mantle field in 4 1/2-5 weeks was followed by a 3-4 week break and 35-40Gy to the paraaortic field. Daily fraction size was 1.1-1.8Gy. T cell subsets were identified by fluorescent staining of lymphocyte surface antigens using murine monoclonal antibodies OKT3, OKT4, OKT8, and OKT10 (reactive with all T cells, helper/inducer cell (H/I), cytotoxic/suppressor cells (C/S), and activated/immature lymphocytes (A/I), respectively) and quantitated by flow cytometry. Absolute levels of total lymphocytes, H/I, and C/S fell rapidly during LI. H/I declined from 41 +/-8% of lymphocytes prior to LI to 16 +/-5% at 4-5 months post-LI. Percent of C/S cells were not appreciably changed by LI. Of lymphocytes 30+/-8% were C/S prior to LI and 26+/-14% were C/S at 4-5 months post-LI. Based on our understanding of T-PBL changes in Hodgkin's Disease patients, we performed a series of transplantation experiments on 9 previously splenectomized cynomolgus monkeys. We conclude: (1) LI causes depression of T-PBL. (2) Increases in T-PBL of C/S relative to H/I is a feature of T cell subset repopulation. (3) A short LI to surgery interval appears to be a characteristic of successful transplantation. The relatively tolerant state to transplantation following LI was lost by 3 1/2 weeks despite increased T-PBL of C/S relative to H/I. (no Refs)

7. SELECTIVE IMMUNOSUPPRESSION BY TOTAL LYMPHOID IRRADIATION: APPLICATIONS IN AUTOIMMUNE DISEASE AND ORGAN TRANSPLANTATION (MEETING ABSTRACT).

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Division of Radiation Therapy, Stanford University Medical Center, Stanford, CA, 94305

Twenty-fourth Annual Meeting of the American Society of Therapeutic Radiologists, October 25-29, 1982, Orlando, Florida American Society of Therapeutic Radiologists; 1982

The technique of total lymphoid irradiation (TLI) was developed at Stanford in 1962 for the treatment of patients with Stage III Hodgkin's disease and other malignant lymphomas. Long term observations are now available on hundreds of patients treated by this technique to essentially all of the lymphoid tissues of the human body. The only clinically overt immunologic effects of TLI have been an increase in susceptibility to herpes zoster-varicella virus infection and one well-documented case of radiation-induced splenic atrophy, complicated by fatal pneumococcal sepsis. In vitro studies revealed that TLI induces a profound T-lymphocytopenia which may persist for 10 years or more after successful radiotherapy for Hodgkin's disease. The T-lymphocytopenia is accompanied by profound abnormalities of T-lymphocyte reaction which may persist for 2-5 years and an impairment of responses to PHA and other lectins which may persist for 10 or more years. These observations suggested that TLI might be useful as an immunosuppressive regimen for patients undergoing organ and tissue transplantation, as well as in patients with severe autoimmune disease. Laboratory investigations in mice, rats, dogs, and monkeys have confirmed the remarkable efficacy of TLI as a conditioning regimen in organ and tissue recipients. The cellular mechanisms underlying these immunosuppressive effects of TLI have been extensively investigated and point strongly to the induction of populations of suppressor cells which block both host-vs-graft and graft-vs-host reactions. Preliminary clinical investigations are now in progress to assess the efficacy of TLI in the treatment of patients with refractory rheumatoid arthritis and with systemic lupus erythematosus and impaired renal function, as well as in patients undergoing organ transplantation. (no Refs)

HODGKIN'S DISEASE: MULTIMODAL THERAPY

8. HODGKIN'S DISEASE LIMITED TO INTRATHORACIC SITES (MEETING ABSTRACT).

Johnson DW, Hoppe RT, Cox RS, Kaplan HS
Department of Radiology, Stanford University Medical Center, Stanford, CA, 94305
Twenty-fourth Annual Meeting of the American Society of Therapeutic Radiologists, October 25-29, 1982, Orlando, Florida American Society of Therapeutic Radiologists; 1982

The records of 1470 patients (pts) treated for Hodgkin's disease between 1960 and 1980 were reviewed and sites of initial involvement were noted. Among these pts, 43 had disease limited to intrathoracic sites after completion of clinical staging. All pts were treated with irradiation (XRT) to involved field (IF), mantle (M), subtotal nodal (S), or total lymphoid (TL) fields. Pts with pulmonary hilar node involvement received low dose (1500-1650 rad) prophylactic ipsilateral lung XRT. Eighteen pts were also treated with adjuvant chemotherapy, consisting of nitrogen mustard, vincristine, procarbazine, +/- prednisone (MOP(P)), or procarbazine, melphalan, and vinblastine (PAVe). The median age was 28 yr (range 12-66) and the male:female ratio was 1:1.2. The histologic subtype was nodular sclerosis in 40 cases (91%), mixed cellularity in 1, and unclassifiable in 3. The median followup was 7.5 yrs. The actuarial survival at 5 and 10 years was 93% and 89%, respectively, and the freedom-from-relapse (FFR) at 5 and 10 years was 81% and 78%, respectively. Nine pts relapsed, all above the diaphragm (5 within lung parenchyma). Seven had initially received XRT alone, and two had received combined-modality treatment. The risk of relapse in the 26 pts treated with XRT alone varied inversely with the volume irradiated: IF=100% (3/3), M=28% (2/7), S=16% (2/12), TL=0% (0/4), relapsed. Six of the seven relapsing pts treated with XRT alone were salvaged with subsequent XRT and/or chemotherapy, whereas both of the combined-modality pts who relapsed ultimately died with progressive disease. Of the 5 pts with lung relapses, one had received prophylactic XRT to that lung. Hodgkin's disease clinically limited to intrathoracic sites was uncommon (3% of presentations), but survival and FFR for this group were excellent. If patients were treated with XRT alone, prophylactic lung irradiation appeared to decrease the incidence of lung relapse. Relapses occurred exclusively in supradiaphragmatic sites, and reflect inadequate control of local-regional disease. (no Refs)

9. THE ROLE OF RADIOTHERAPY IN THE TREATMENT OF ADVANCED HODGKIN'S DISEASE (A RANDOMIZED STUDY OF CANCER AND LEUKEMIA GROUP B - CALGB) (MEETING ABSTRACT).

Rafla S, Coleman M, Pajak T, Vinciguerra V
Methodist Hospital, Brooklyn, NY
Twenty-fourth Annual Meeting of the American Society of Therapeutic Radiologists, October 25-29, 1982, Orlando, Florida American Society of Therapeutic Radiologists; 1982

CALGB embarked on a multimodal randomized study to compare the additive effect of radiotherapy (given to bulky disease) to a standard six course of four drug therapy (CCNU (lomustine), vinblastine, procarbazine and prednisone-CVPP) and to augmented cycles of chemotherapy (12 cycles). Radiotherapy (2500 rads in 4 weeks) was delivered either after six courses of CVPP or sandwiched between 2 sets of three courses of CVPP. Three hundred and five patients were included with 244 evaluable distributed evenly among the 4 arms. About two-thirds of patients were men. Survival results at 60 months favor the sandwich therapy arm (78% versus 50% after the standard six cycles) with best results in younger patients (less than 40) who were included after the modification of the length of treatment period (no failure in 24 months follow-up period). A study of patterns of failure in all patients who received radiotherapy revealed that 71% (29 of 98) continued to enjoy relapse-free survival. After removing the 8 cases that failed without disease recurrence (refusal to continue on study, death due to unrelated causes, etc) the failure rate is reduced to 23% (21 of 90). The majority of failures (15 of 21) occurred in unirradiated neighboring sites, mostly nodal. Organ failure occurred only in 30% of cases distributed among liver, spleen, lung and skin. In-field recurrences occurred in 6 of 98 patients (6%) presenting primarily as large mediastinal masses growing to involve sternum and skin or organ recurrences (liver or spleen). (no Refs)

10. TREATMENT OF GENERALIZED HODGKIN'S DISEASE IN CHILDREN.

Vialushkin BIa, Koshel' IV, Tsyplenkov VG
Inst. Pediatrics, Moscow, USSR
Pediatriia; (6):49-52 1982

Results of treatment of 81 children (3-15 yr old) who had generalized Hodgkin's disease (HD) are reported. Twenty-one of these patients were in Stage IIIA, and 60 were in Stage IIIB; 9 had lymphoid predominance, 11 had nodular sclerosis, 49 had mixed variant, and 12 had lymphoid depletion. Prior to chemotherapy, the patients were subjected to exploratory laparotomy with splenectomy, biopsy of enlarged lymph nodes, and marginal liver biopsy. Histological examination showed spleen involvement in greater than 70% of the patients. Induction therapy included administration of cyclophosphamide (600 mg/square meter, iv, days 1 and 8), vinblastine (15 mg/square/meter, iv, days 1 and 8), procarbazine (100 mg/square meter, po, daily), and prednisone (40 mg/square meter, po, daily). The patients received six 2-wk courses of the polychemotherapy with 10-14 days between the courses. Complete remission was achieved in greater than 95% of the patients. Maintenance therapy included distance gamma irradiation (3,500-4,500 rads to the primary focus and 3,200-4,000 rads to zones of regional metastatic spread). The 5-yr survival rate was 92.7%; 54.6% of the patients were free of recurrences. (no Refs) (In RUS)

11. EORTC (EUROPEAN ORGANIZATION FOR RESEARCH ON TREATMENT OF CANCER) STUDY OF HODGKIN'S DISEASE.

Somers R, Burgers JMV, Hartgrink-Groeneveld CA, Kazem I, Noordijk EM, Qasim MM, Sizoo W, Van Unnik JAM, Wagener DJTh
Antoni van Leeuwenhoek Ziekenhuis, Amsterdam, The Netherlands
Ned Tijdschr Geneeskd; 126(14):616-622 1982

The results of two clinical trials in patients with Hodgkin's disease Stage I and II are presented. The first trial during the period 1964-1971, ie, before the introduction of staging laparotomy and polychemotherapy, include 153 patients subjected to radiotherapy and 136 subjected to radiotherapy and to chemotherapy with vinblastine. The incidences of recurrence were 58% in the radiotherapy group and 37% in the combination therapy group (p less than 0.01), and the 5-yr symptom-free survival rates were significantly higher after combination therapy than after radiotherapy only, even though the difference in the overall 5-yr survival rates was not significant. Recurrences developed in the irradiated area in 11% of the patients subjected to radiotherapy only, and in 6% of those subjected to combination therapy. The survival rates were significantly higher (p less than 0.005) in the patients with favorable prognoses than in those with unfavorable prognoses. The second trial during the period 1971-1976 included 131 patients (Group I) subjected to radiotherapy only (mantle-field irradiation) and 125 (Group II) subjected to staging laparotomy with splenectomy, followed by mantle-field irradiation. Splen involvement was found in 37/125 laparotomized patients. The incidences of recurrences were 33% in Group I, 20% in the 88 patients without and 46% in those with spleen involvement in Group II. The symptom-free survival rate was found to be lowest for the patients with spleen involvement. Extended irradiation involving the upper abdomen had favorable effect on both the overall and symptom-free survival rates in the patients with favorable and unfavorable prognostic signs alike compared with the first trial. (10 Refs) (In DUT)

HODGKIN'S DISEASE: CASE REPORTS

12. PRIMARY KAPOSI'S SARCOMA AND HODGKIN'S DISEASE IN THE SAME LYMPH NODE.

Massarelli G, Tanda F, Denti S
Inst. Morbid Anatomy, Univ. Sassari, Via Matteotti 58, I-07100 Sassari, Italy
Am J Clin Pathol; 78(1):107-111 1982

The occurrence of primary Kaposi's sarcoma in a lymph node affected by Hodgkin's disease is reported. The case concerns a 43-year-old woman with a recurrence of Hodgkin's disease 13 years after its initial diagnosis. In one of four excised supraclavicular nodes a Kaposi's sarcoma was unexpectedly found. The present observation stresses once more that the two diseases are closely related and possibly share the same pathogenesis. (Author abstract) (35 Refs)

HODGKIN'S DISEASE: SELECTED REPORTS ON ETIOLOGY AND EPIDEMIOLOGY

13. WARTHIN-FINKELDEY-LIKE CELLS IN BENIGN AND MALIGNANT LYMPHOID PROLIFERATIONS.

Delsol G, Pradere M, Voigt JJ, Nespoulous M, Gorguet B, Marty C, Fabre J
Laboratoire d'Anatomie Pathologique, CHU PURPAN, Place du Dr. Baylac, 31059 Toulouse Cedex, France
Histopathology; 6(4):451-465 1982

A search was conducted of routine biopsy specimens of Hodgkin's disease (337), non-Hodgkin's malignant lymphoma (26), pseudolymphomas of the orbit (6), and benign and malignant lymphoid proliferations (2) for Warthin-Finkeldey-like cells (WFLC) that in many respects resembled the cells originally described by Warthin and Finkeldey as associated with measles. Measles infection was not clinically suspected in any of the cases studied. Light and transmission electron microscopy revealed consistent morphological characteristics that allowed the WFLC to be classified into three main types by light microscopic characteristics and two types by electron microscopic characteristics. WFLC were found in 19/337 cases of Hodgkin's disease, with 14/17 in cases exhibiting nodular lymphocytic predominance. WFLC were mainly observed within germinal centers and in B-cell lymphomas. In five cases studied, immunoperoxidase staining showed a negative reaction for immunoglobulins, lysozyme, alpha 1 anti-chymotrypsin, and alpha 1 antitrypsin in WFLC. The origin of WFLC in lymphoid disorders is unknown; it may be due to reactivation of an endogenous virus as a result of favorable conditions produced by the lymphoproliferative process or reinfection by an exogenous virus. (22 Refs)

MALIGNANT LYMPHOMA: DIAGNOSIS AND STAGING

14. MORPHOLOGIC TYPES OF DIFFUSE LARGE-CELL LYMPHOMA.

Warnke RA, Strauchen JA, Burke JS, Hoppe RT, Campbell BA, Dorfman RF
Dept. Pathology, Stanford Univ. Medical Center, Stanford, CA, 94305
Cancer; 50(4):690-695 1982

One hundred eighty-seven patients with confirmed diffuse non-Hodgkin's lymphoma were selected from a consecutive series of 391 patients who were evaluated and treated at Stanford University Medical Center. Lymphomas with any degree of nodularity and diffuse lymphomas of 'well-differentiated' and 'poorly differentiated' lymphocytic type were excluded from this study. Each of four observers identified cases of diffuse large-cell lymphoma from the 187 cases and further subdivided these cases into six morphologic types in accordance with criteria proposed by Strauchen et al. Initial intraobserver and interobserver agreement was relatively low but was greatly enhanced when the initial six morphologic types were grouped as either follicular center-cell or nonfollicular center-cell types. When individual observer results were pooled, statistically significant differences were 88een between survival of patients in these two groups, with the patients in the nonfollicular center-cell group having a worse prognosis ($p = 0.04$). This effect of morphologic type appeared to be independent of pathologic stage. Mitotic counts did not correlate with survival. (Author abstract) (20 Refs)

15. NON-HODGKIN'S LYMPHOMAS - NODULAR HISTOLOGY THE PRINCESS MARGARET HOSPITAL EXPERIENCE (MEETING ABSTRACT).

Gospodarowicz MK, Brown TC, Bush RS
Princess Margaret Hospital, Toronto, Ontario, Canada
Twenty-fourth Annual Meeting of the American Society of Therapeutic Radiologists, October 25-29, 1982, Orlando, Florida American Society of Therapeutic Radiologists; 1982

From 1967 to 1978 1,394 patients with Non-Hodgkin's lymphomas were treated at the Princess Margaret Hospital. Of those 527 patients were classified as nodular lymphomas according to the Rappaport's classification. Overall actuarial survival was 45% at 10 years and relative survival was 54%. Patients ranged in age from 18 to 87 years of age, with the median being 56 years of age. Important prognostic factors included age with the 60% 10 year actuarial survival for patients less than 60 years of age and a median survival of 4 years. Stage was an important prognostic factor, with stage IA-3A achieving 54% 10 years actuarial survival and a median survival of 12 years and stage IB-3B and 4 patients -21% 10 years actuarial survival and a median survival of 3 years. Bulk of the disease was an important prognostic factor, while histology was not. Patients with stage IA and 2A localized nodular lymphoma with small bulk of tumor achieved 90% 10 years actuarial survival with 78% failure free rate and represent a group highly curable with irradiation. (no Refs)

16. SKELETAL CHANGES IN NON-HODGKIN'S LYMPHOMAS.

Spanedda R, Scutellari PN, Marinelli G, Orzincolo C, Cervi PM
Cattedra di Ematologia, Universita degli Studi di Ferrara, Ferrara, Italy
Minerva Med; 73(25):1769-1774 1982

Skeletal changes were studied in 140 patients (86 men and 54 women, 22-82 yr old) with non-Hodgkin's lymphomas. Favorable histological types of lymphoma were diagnosed in 105/140 patients, unfavorable types in 35/105. Bone involvement was evidenced clinically, radiologic, biologically and scintigraphically in 14/140 patients (4 men and 10 women, 52-82 yr old). The skeletal changes were metastatic in all patients and did not appear as initial symptoms in any of them. Osteolytic changes were found radiologically in 7/14 patients, rarefaction in 5/14 and sclerotic and mixed changes in 1/14 each. The skeletal changes were solitary in 13 patients and triple in 1. The triple bone lesions were osteolytic. The cranium, paranasal sinuses and facial bones were affected in two patients, the vertebral column in four, the rib and shoulder girdle in one each, the pelvic bones in six and the femur in two. Diffuse histiocytic lymphoma was diagnosed in 5/14 patients, diffuse mixed histiocytic lymphoma in 4/14 and diffuse poorly differentiated lymphocytic lymphoma in 5/14. Periosteal lesions were not observed in any of the 14 patients. (23 Refs) (In ITA)

17. THE LUKES AND COLLINS CLASSIFICATION OF NON-HODGKIN'S LYMPHOMAS. 2. A SURVIVAL STUDY OF 301 PATIENTS.

Aine R, Alavaikko M, Kataja M
Dept. Pathology, Tampere Univ. Central Hosp., 33520 Tampere 52, Finland
Acta Pathol Microbiol Immunol Scand [A]; 90(4):251-256 1982

In a retrospective study of 301 non-Hodgkin's lymphoma patients the clinical and prognostic value of the classification of Lukes and Collins was studied. A slight majority of the cases were of the follicular center cell types. Stages III-IV were found in 46% of the entire group at the time of diagnosis. The lymphomas showing follicular center cell types were frequently localized (63%). About 65% of all cases survived 1 yr and about 45% 5 yr. The females showed a better survival. The nodal lymphoma cases had the poorest survival. Two prognostically different subgroups of non-Hodgkin's lymphomas were discerned. The more favorable group consisted of the small cleaved FCC type (5-yr relative survival 74%), the small lymphocytic type (62%) and the plasmacytoid lymphocytic type (51%). The small non-cleaved FCC type, the large non-cleaved FCC type and the immunoblastic sarcoma type formed the other group with a less favorable prognosis. Mortality due to these types manifested itself to a level of 65% in the first 2 yr. (Author abstract) (26 Refs)

18. THE LUKES AND COLLINS CLASSIFICATION OF NON-HODGKIN'S LYMPHOMAS. 1. A HISTOLOGICAL REAPPRAISAL OF 301 CASES.

Alavaikko M, Aine R
Dept. Pathology, Oulu Univ. Central Hosp., 90220 Oulu 22, Finland
Acta Pathol Microbiol Immunol Scand [A]; 90(4):241-249 1982

Cytomorphological categories of the Lukes and Collins classification could be recognized in 92% out of a retrospective series of 301 non-Hodgkin's lymphomas. The follicular center cell (FCC) group constituted the majority (54%). Certain differences between the cytological subgroups were observed as regards age and sex and the growth pattern. Follicular features in the growth pattern were found in 16% of the cases. The large cleaved FCC type behaved differently from the other FCC types in many respects. The occurrence of cleaved FCC lymphomas appeared to be exceptional in childhood. There were no small lymphocytic and plasmacytoid lymphocytic lymphomas in children or young adults, and large non-cleaved FCC lymphomas and immunoblastic sarcomas were rare in these. In the small non-cleaved FCC group both the Burkitt type and the non-Burkitt type exhibited a bimodal age distribution with a peak under 10 yr of age and another at age 60-70 yr. Five convoluted lymphocyte lymphomas, between 2 and 29 yr of age, were found in this series. The heterogeneous group of unclassified lymphomas included as a special case one lymphoma with deeply multilobated nuclei. (Author abstract) (24 Refs)

19. CRANIAL COMPUTED TOMOGRAPHY IN THE TUMOROUS STAGE OF MYCOSIS FUNGOIDES.

Vitek JJ, Duvall ER
Div. Neuroradiology, Dept. Diagnostic Radiology, Univ. Alabama in Birmingham, 619 South 19th St., Birmingham, AL, 35233
J Comput Assist Tomogr; 6(4):702-705 1982

Central nervous system (CNS) involvement by mycosis fungoides (MF) is rare. This is especially true of metastatic parenchymal involvement. Findings in two patients having the tumorous stage of MF are described. Multiple, well delineated, homogeneously and markedly enhancing nodules were seen in these two patients. The computed tomographic (CT) features of CNS involvement by MF are not specific. The differential diagnosis is discussed. By using CT in patients with MF, we will eventually be able to determine the incidence of CNS involvement in this condition. (Author abstract) (16 Refs)

MALIGNANT LYMPHOMA: CLINICAL IMMUNOLOGY AND IMMUNOTHERAPY

20. PHENOTYPIC CHARACTERIZATION OF SKIN-INFILTRATING T CELLS IN CUTANEOUS T-CELL LYMPHOMA: COMPARISON WITH BENIGN CUTANEOUS T-CELL INFILTRATES.

Haynes BF, Hensley LL, Jegasothy BV
Duke Univ. Sch. Medicine, Box 3258, Durham, NC, 27710
Blood; 60(2):463-473 1982

Using a panel of monoclonal antibodies, we have studied cell surface antigens of infiltrating mononuclear cells in skin biopsies from patients with cutaneous T-cell lymphoma (CTCL) and compared them with the T-cell surface phenotype seen in benign cutaneous T-cell infiltrations (eg, contact dermatitis, delayed hypersensitivity skin tests, granuloma annulare) and in dermal infiltrates of lymphomatoid granulomatosis patients. We found that unlike circulating CTCL (Sezary) cells, CTCL cells infiltrating skin epidermis frequently expressed the T-cell antigen 3A1. Cutaneous infiltrates in 10 patients with mycosis fungoides (MF) and 1 patient with Sezary syndrome were OKT4 (inducer T cell), OKT8 (suppressor/cytotoxic T cell); 2 patients with MF were OKT4, OKT8; and 1 MF patient's skin T cells were OKT4, OKT8. Similar to CTCL infiltrating cells, most of the benign skin T-cell infiltrates were usually 3A1+, OKT4+, and OKT8+. Our study shows the complex nature of T-cell antigen patterns in inflammatory and malignant skin T-cell infiltrations. We demonstrated that in CTCL the skin epidermal infiltrating T-cell phenotype is not invariate, and in many cases, is similar to the phenotype of clinically benign cutaneous T-cell infiltrations. (Author abstract) (37 Refs)

21. CELLULAR ORIGIN OF HUMAN LYMPHOID MALIGNANCIES AS BASED ON IMMUNOLOGIC ANALYSIS OF MEMBRANE DIFFERENTIATION ANTIGENS.

Tobinai K, Hirose M, Yamada H, Minato K, Shimoyama M
(c/o Shimoyama) Section of Hematology, Natl. Cancer Center Hosp., 1-1, Tsukiji 5-chome, Chuo-ku, Tokyo 104, Japan
Jpn J Clin Oncol; 12(1):73-90 1982

Cell surface antigens of 80 patients with human lymphoid malignancies were analyzed with the aid of 11 monoclonal antibodies, and their cellular origins were determined according to the expression of differentiation antigens. The lymphoid malignancies included 33 cases of T-cell malignancy [5 acute lymphoblastic leukemias (ALL) and 28 lymphomas] and 47 cases of non-T cell malignancy (15 ALL and 32 lymphomas). The T-cell malignancies were divided into four major categories. Two cases of ALL were classified as pre-T cell type. Two cases of ALL and five cases of lymphoblastic lymphomas were classified as early thymocyte subtype of thymic T-cell type. One case of ALL was classified as common thymocyte subtype of the thymic T-cell type. Seven cases of adult T-cell leukemia, five of medium size and large cell type lymphoma, one of chronic lymphoblastic lymphoma (CLL), and one of mycosis fungoides were classified as inducer/helper T-cell type. Five other cases of T-cell malignancy were classified as suppressor/cytotoxic T-cell type. Cellular origins of four cases could not be determined. Of the 47 cases of non-T cell malignancy, 15 were peroxidase-negative. These 15 included one case classified as null cell type, two classified as unknown type with Ia-like antigen, eight classified as lymphoid stem cell type, two classified as pre-B cell type, and two classified as immature B-cell type. Mature B-cell phenotype was expressed in 26/32 non-T cell lymphomas. Five cases of medium and large cell type non-Hodgkin's lymphoma expressed the pre-B cell phenotype. L1-or L2-morphological classification of cases of ALL did not correlate with cellular origin, but most cALL antigen-positive cases of ALL were classified as L1-morphology. (50 Refs)

22. DEMONSTRATION OF IMMUNOGLOBULIN IN MALIGNANT LYMPHOMAS. USE OF AN IMMUNOPEROXIDASE TECHNIC ON FROZEN SECTIONS.

Harris NL, Poppema S, Data RE
Immunopathology Unit, Massachusetts General Hosp., Boston, MA, 02114
Am J Clin Pathol; 78(1):14-21 1982

We used an immunoperoxidase technic to detect surface and cytoplasmic immunoglobulin in frozen sections of 46 malignant lymphomas. With the immunoperoxidase technic, differential staining with antisera to the various heavy and light chain classes permitted detection and characterization of monotypic immunoglobulin in frozen sections of 15 of 15 nodular lymphomas and 24 of 31 diffuse lymphomas. The immunoperoxidase technic applied to frozen sections is a convenient and reliable method for the detection of immunoglobulin in lymphoid tissues, which can be performed in a pathology laboratory without the need for special equipment. (Author abstract) (28 Refs)

MALIGNANT LYMPHOMA: CHEMOTHERAPY

23. COMBINATION CHEMOTHERAPY WITH CYCLOPHOSPHAMIDE, VINCRISTINE, PREDNISONE AND THE CONTRIBUTION OF ADRIAMYCIN IN THE TREATMENT OF ADULT NON-HODGKIN'S LYMPHOMAS. A REPORT OF 131 CASES.

Parlier Y, Gorin NC, Najman A, Stachowiak J, Duhamel G
Dept. Hematology, Hopital Saint-Antoine, 75571 Paris Cedex 12, France
Cancer; 50(3):401-409 1982

Between January 1973 and January 1979, 131 patients with malignant non-Hodgkin's lymphomas were treated with cyclophosphamide-vincristine-prednisone either alone or combined with Adriamycin (CVP-A). Stage I and II lymphocytic lymphomas were all treated by CVP combined with radiotherapy. The survival curve for this group of patients plateaued at 89% from the 12th to the 60th mo, which was the endpoint of the study. For Stage III and IV nodular lymphocytic lymphomas, actuarial survival was 69% at 5 years in the CVP-treated group as compared to 54% at 3 years in the group treated with CVP-A. For Stage III and IV diffuse lymphocytic lymphomas, the complete response rate and median survival were respectively 25% and 24 mo in patients treated with CVP, as compared to 67% (p less than 0.01) and 26 mo in the group treated with CVP-A. For histiocytic lymphomas, the complete response rate was 50% in the CVP-treated group as compared to 83% in the group treated with CVP-A. Most remarkable was the fact that while in the CVP treated group median survival was only 17 mo, the small group of patients treated with CVP-A exhibited considerably improved survival with a horizontal survival curve at 90% after 36 mo. These results show that the CVP protocol remains an excellent treatment for nodular lymphocytic lymphomas. The addition of Adriamycin (CVP-A) as well as its inclusion in other drugs combination, has raised hopes for remissions of long duration and even for cures in patients with histiocytic lymphomas. Finally, in diffuse lymphocytic lymphomas, efforts will have to be pursued to improve the prognosis which remains poor despite the increased complete response rate achieved by the addition of Adriamycin. (Author abstract) (20 Refs)

24. COMBINATION CHEMOTHERAPY OF ADVANCED DIFFUSE HISTIOCYTIC LYMPHOMA WITH THE SIX-DRUG COP-BLAM REGIMEN.

Laurence J, Coleman M, Allen SL, Silver RT, Pasmantier M
(c/o Coleman), New York Hosp.-Cornell Medical Center, 525 East 68th St., New York, NY, 10021
Ann Intern Med; 97(2):190-195 1982

A new multiple-drug protocol consisting of cyclophosphamide, vincristine, prednisone, bleomycin, doxorubicin, and procarbazine, known as COP-BLAM, was administered to 48 patients with Stage III or IV diffuse histiocytic lymphoma. Twenty-four of the 33 previously untreated patients had a complete remission, and 8 patients had a partial response. The median survival for all previously untreated patients has not yet been reached at 23 mo. Median survival for complete responders has not yet been attained at 26 mo, although survival of partial responders is 12.5 mo. There were no patients with a complete response who had a central nervous system relapse. The COP-BLAM therapy is an easily administered outpatient program capable of inducing a high frequency of durable complete remissions in advanced diffuse histiocytic lymphoma, a malignancy formerly considered to have a poor prognosis. (Author abstract) (24 Refs)

25. THE USEFULNESS OF THE LUKES-COLLINS CLASSIFICATION IN IDENTIFYING SUBSETS OF DIFFUSE HISTIOCYTIC LYMPHOMA RESPONSIVE TO CHEMOTHERAPY.

Newcomer LN, Nerenberg MI, Cadman EC, Waldron JA, Farber LR, Bertino JR
(c/o Cadman), Yale Univ. Sch. Medicine, P. O. Box 3333, 333 Cedar St., New Haven, CT, 06510
Cancer; 50(3):439-443 1982

Twenty-nine patients with Stage III and IV diffuse histiocytic lymphoma (DHL) were treated prospectively with cyclophosphamide, hydroxydaunorubicin, vincristine, prednisone and bleomycin (CHPO-B) or hydroxydaunorubicin, cyclophosphamide, vincristine, methotrexate with leucovorine rescue and cytosine arabinoside (ACOMLA). Twenty-six evaluable patients were reclassified blindly by the Lukes-Collins classification with five large noncleaved follicular center cell (FCC), six large cleaved FCC, three large cell unclassified, seven B-immunoblastic sarcoma and five T-immunoblastic sarcoma patients identified. There was no significant survival advantage between the two combination chemotherapy programs. Survival of the immunoblastic sarcoma patients was inferior to that of the FCC lymphoma patients ($p = 0.02$). There were no significant survival differences between the large cleaved FCC and noncleaved FCC subtypes. Immunoblastic sarcomas, B- and T-cell types, appear to be more resistant to standard combination chemotherapy programs and new approaches may warrant more aggressive therapy in future protocols. The large cell FCC lymphomas have an excellent prognosis. (Author abstract) (12 Refs)

MALIGNANT LYMPHOMA: RADIOTHERAPY

26. PATHOLOGIC FRACTURE AFTER RADIATION THERAPY FOR PRIMARY NON-HODGKIN'S MALIGNANT LYMPHOMA OF BONE (MEETING ABSTRACT).

Stokes SH, Walz BJ
Division of Radiation Oncology, Washington University School of Medicine, St. Louis, MO
Twenty-fourth Annual Meeting of the American Society of Therapeutic Radiologists, October 25-29, 1982, Orlando, Florida American Society of Therapeutic Radiologists; 1982

Between 1963 and 1981, 32 patients with biopsy proven non-Hodgkin's lymphoma involving bone were treated at the Mallinckrodt Institute of Radiology either with radiation alone or in conjunction with chemotherapy. An unexpectedly high rate of fracture at the site of the tumor was observed. Six patients were excluded because they survived less than six months after the completion of radiotherapy or were lost to follow-up within six months. There were 15 appendicular and 17 axial sites treated. Local control was achieved in 30 of 32. Twenty-six sites of involvement received less than 5000 rad. Five sites of involvement with diffuse histiocytic lymphoma (DHL) involving the appendicular skeleton received 5000 to 6000 rad. One site with DHL involving the axial skeleton received 5000 rad. Of the six patients receiving high dose, two presented with pathologic fractures of the femur requiring surgical stabilization and the remaining four patients suffered subsequent fractures 7 to 30 months after completion of therapy. Two of these six had local recurrence of disease. It appears that doses of 5000 rad or greater do not increase the probability of local control but may substantially increase the risk of fracture following radiotherapy in lymphoma of the bone. (no Refs)

27. TOTAL SKIN ELECTRON IRRADIATION (TSEI) FOR MYCOSIS FUNGOIDES (MF): FAILURE ANALYSIS AND PROGNOSTIC FACTORS (MEETING ABSTRACT).

Tadros A, Tepperman B, Hryniuk W, Peters V
Ontario Cancer Foundation Clinic, Hamilton, Ontario, Canada
Twenty-fourth Annual Meeting of the American Society of Therapeutic Radiologists, October 25-29, 1982, Orlando, Florida American Society of Therapeutic Radiologists; 1982

From 1970 to 1980, 106 patients with MF were treated by TSEI. A 6-field technique with 3 MeV electrons at 7 m SDD delivered a total skin dose of 20-35 Gy in 2-4 weeks. Eighty-eight patients had failed prior treatments. Fifty patients had cutaneous plaques only (T1N0-7; T2N0-43), and 56 more advanced stages (T2N+ -20; T3-26: T4-10). Men predominated 41:22 in stage T2 and 37:6 in all other stages. Follow-up ranged to 143 months, with a median of 30 months. Complete response was more frequent in stages T1-2N0 (48/50 vs 40/56). In advanced stages, complete responses were more frequent with doses over 25 Gy (32/40 vs 8/16). Of 15 patients in continuous complete remission for over 48 months, only one has relapsed. Following adequate TSEI (over 25 Gy), there were 49 relapses among 69 complete responders of all stages. Of these, 45 (92%) failed first in skin, and 91% of these involved sites of previous lesions or shielded areas. Extracutaneous progression following TSEI was seen in 6% of patients with plaque disease and 48% with advanced disease. In T1-2N0, extracutaneous progression occurred exclusively with doses under 30 Gy (21%). In advanced stages, risk of extracutaneous progression increased with age over 55 (63% vs 21%). In all stages, death with MF correlated only with extracutaneous progression (64% vs 1.8%). TSEI can produce prolonged complete regressions of MF. Nevertheless, specific subsets-for example, patients over 55 (almost exclusively males) presenting with advanced disease-may benefit from adjuvant therapy. (no Refs)

28. PALLIATIVE RADIATION TREATMENT OF CUTANEOUS MYCOSIS FUNGOIDES - A DOSE RESPONSE (MEETING ABSTRACT).

Cotter GW, Baglan RJ, Wasserman TH, Mill W
Mallinckrodt Institute of Radiology, Washington University School of, Medicine St. Louis, MO
Twenty-fourth Annual Meeting of the American Society of Therapeutic Radiologists, October 25-29, 1982, Orlando, Florida American Society of Therapeutic Radiologists; 1982

Between 1966 and 1981, 20 patients (191 lesions) underwent palliative radiation therapy for control of biopsy proven cutaneous mycosis fungoides. Six patients (47 lesions) and an additional 34 lesions from the remaining 14 patients with complete response to treatment were excluded from the study due to followup of less than one year. Included in the remaining 110 lesions were all recurrences and all partial responses. The modalities for treatment included superficial, Cobalt-60 or electron beam irradiation. The total tumor doses employed ranged from 600-4000 c Gray. The 110 lesions (14 patients) were retrospectively analyzed to determine the dose required for local control of the lesions. Fifty-three percent of the lesions were classified as plaques, 20% as tumors less than 3 cm in diameter, and 27% as tumors greater than 3 cm in diameter. Complete response to treatment was observed in 95% of the plaque lesions, 95% of the tumors less than 3 cm in diameter and 93% of tumor greater than 3 cm in diameter. A complete response to treatment was noted in all lesions receiving greater than 2000 c Gray. In the total population of lesions having a complete response, a local infield recurrence rate of 35% was noted in the group receiving less than 1000 c Gray, 33% in those receiving 1001-2000 c Gray, 29% in those receiving 2000-3000 c Gray, and 0% in the group receiving greater than 3000 c Gray. Of those lesions which recurred, the mean time to recurrence for the first three dose ranges above were respectively, 4.7 months, 9 months and 16 months. Eighty-three percent of the 30 recurrences were seen within one year of treatment; 100% of the recurrences occurred within two years of treatment. The data from this study indicate that tumor doses greater than 3000 c Gray are needed for adequate local control of cutaneous mycosis fungoides. There is, however, no evidence that doses in excess of 4000 c Gray are of additional benefit. (no Refs)

MALIGNANT LYMPHOMA: MULTIMODAL THERAPY

29. EXTRALYMPHATIC INVOLVEMENT IN DIFFUSE NON-HODGKIN'S LYMPHOMA (MEETING ABSTRACT).

Paryani SB, Sneed P, Dawley D, Hoppe RT, Burke JS, Cox RS, Rosenberg SA, Kaplan HS

Department of Radiology, Stanford University Medical Center, Stanford, CA, 94305

Twenty-fourth Annual Meeting of the American Society of Therapeutic Radiologists, October 25-29, 1982, Orlando, Florida American Society of Therapeutic Radiologists; 1982

Between 1961 and 1982, 543 patients were treated for diffuse histiocytic (DH), diffuse mixed histiocytic-lymphocytic (DM), and diffuse undifferentiated (DU) lymphoma. Of this group of patients, 281 (52%) had extralymphatic (E) lesions utilizing strict Ann Arbor staging criteria. Patients with stage III and IV disease were excluded leaving 116 patients with stage IE and IIE disease for analysis. Initial staging studies included lymphangiography in 77%, bone marrow biopsy in 91%, and diagnostic or staging laparotomy in 52% of patients. All except five patients were treated with megavoltage irradiation to either involved field (IF), extended field (EF), or total lymphoid (TLI) fields to a total dose of 3500-5000 rad. In addition, 36 patients received combination chemotherapy. Median followup was 4.0 years. Kaplan-Meier actuarial survival at 5 and 10 years was 46% and 40%, respectively. Freedom from relapse (FFR) at 5 years was 50% with no relapses beyond that point. Most patients had DH (88%) while only 12% of patients had DM (7%) or DU (5%). There was no significant difference in either survival or FFR among the three histologies. There was no significant difference in either survival or FFR for patients with IF, EF, or TLI. Addition of chemotherapy had no significant impact on either survival or FFR. Males had a significantly worse survival and FFR than females. Patients with bulky abdominal disease (greater than 10cm) had a significantly poorer survival and FFR. However, there was no significant difference in survival or FFR between patients with stage IE or IIE disease. Most patients relapsed within the first two years after treatment with no relapses after 5 years. Most relapses (67%) were in noncontiguous nodal sites or new distant extralymphatic sites. (no Refs)

30. LYMPHOMAS AND PSEUDOLYMPHOMAS OF THE ORBIT (MEETING ABSTRACT).

Rao DV, Cosby K, Smith M, Griffith R

Radiation Oncology, Washington University Medical Center, St. Louis, MO

Twenty-fourth Annual Meeting of the American Society of Therapeutic Radiologists, October 25-29, 1982, Orlando, Florida American Society of Therapeutic Radiologists; 1982

Between 1958 and 1979, 33 patients with orbital lymphomas (20) and pseudolymphomas (13) were diagnosed at Washington University Medical Center, predominant symptoms were proptosis, ocular mass and diplopia. Age of the patients varied from 34 to 91 years. Pathology was reviewed in all patients. All patients had a minimum follow-up of at least two years. A) Lymphomas; Forty percent were lymphocytic and the other 60% included diffuse histocytic, mixed cell, and unclassified varieties. All patients were treated with radiation therapy, 18 as primary therapy, and one patient after surgery, and in one patient after failure with primary chemotherapy. Doses ranged from 400-5500 rad, 85% of the patients receiving over 2000 rad. Ultimate control in orbit was 96%. No dose response was noted beyond 2000 rad, after which no local failures were noted. Among the 13 patients whose disease was limited to the orbit at the time of the diagnosis, four patients (31%) developed disseminated lymphoma. Six of the nine patients who had disseminated disease either at diagnosis or developed later, succumbed to the systemic disease. B) Pseudolymphomas (Benign Lymphoid Hyperplasia); Steroids were used in four patients and surgery in one patient as the primary therapy who had to be treated later with radiation therapy for persistence or progression of orbital disease. Twelve patients (92%) obtained permanent local control with doses ranging from 380-3000 rad, 85% receiving 1000 rad or more. It appears that doses of 1000 rad are adequate to provide permanent control of pseudolymphomas. A small subset of four patients with pseudolymphomas who later developed malignant lymphomas were also treated in the same time span. Two patients received surgery as a primary therapy and both recurred locally in the form of malignant lymphoma. Two other patients who received radiation as the primary therapy developed extraocular malignant lymphoma. Among the four patients, one succumbed to systemic disease and the other three are free of disease, all four having obtained permanent local control. (no Refs)

31. COMBINED MODALITY THERAPY OF MYCOSIS FUNGOIDES (MEETING ABSTRACT).

Ch[illegible] MG, Braverman IM, Cadman EC, Yager NB

Departments of Therapeutic Radiology, Yale University School of Medicine, New Haven, CT, 06510

Twenty-fourth Annual Meeting of the American Society of Therapeutic Radiologists, October 25-29, 1982, Orlando, Florida American Society of Therapeutic Radiologists; 1982

Since 1964, 85 patients with mycosis fungoides (MF) received radiation therapy at Yale-New Haven Hospital. After 1973, 20 patients with mostly limited and generalized plaque disease were treated with curative intent by a modified Stanford technique: 3-6 MeV electrons, 100 rads per day to 3600 rads total. Complete remissions were achieved in 18 of these 20 patients. Contrary to the Stanford results, however, only 4 patients (20%) have remained without evidence of disease, most of the others relapsing within 2 years of initial therapy. Because of the high relapse rate from aggressive electron beam therapy in this center, and because of recent evidence suggesting seeding of MF cells from extracutaneous sites, we have been investigating the usefulness of a new treatment regimen of electron beam therapy and adjuvant chemotherapy. Since 1979, 21 patients with newly diagnosed MF (mostly eczematous and limited plaque disease) and 2 patients with relapsed MF following prior radiation therapy have been treated by this protocol. Staging studies include skin and bone marrow biopsies, karyotype and banding analyses of cultured skin, lymph node and peripheral blood cells, serum immunoglobulins, liver/spleen scan, abdominal CT, (computed tomography) and directed lymh node biopsy of palpable lymph nodes or 'blind' biopsy of regional lymph nodes. The treatment regimen consists of 3600 rads whole skin 6 MeV electron beam radiotherapy (6 fields) with split course 2000 rads orthovoltage boost to shielded sites (soles of feet and perineum), followed in 1 month by adriamycin 30 mg/m2 iv and cyclophosphamide 100 mg/m2 po x 14 days, monthly, for 6 months. One-third of the patients are more than two years post-completion of therapy, and all remain in complete remission. No untoward side-effects from the combined theapy have been encountered. Results of the staging studies and karyotype analyses will also be presented. The current data suggest substantially better disease-free survival compared to radiotherapy alone controls. (no Refs)

32. ORAL RETINOID IN COMBINATION WITH BLEOMYCIN, CYCLOPHOSPHAMIDE, PREDNISONE AND TRANSFER FACTOR IN MYCOSIS FUNGOIDES.

Zachariae H, Grunnet E, Thestrup-Pedersen K, Molin L, Schmidt H, Starfetl F, Thomsen K
Dept. Dermatology, Marselisborg Hosp., Univ. Aarhus, Aarhus, Denmark
Acta Derm Venereol (Stockh); 62(2):162-164 1982

Oral retinoids seem to have been of great benefit in a non-randomized study on advanced mycosis fungoides using two different chemotherapy regimens, one with retinoid, the other without. Both groups also received a three-drug chemotherapy with bleomycin, cyclophosphamide and prednisone. Complete remission including all signs of lymph-node involvement was found in 8 of 10 patients of the retinoid treated group, while none went into complete remission in the control group. All in the control group died between 3 and 12 mo after therapy, whereas all but one in the retinoid treated group are alive. Other treatment differences between the groups were related to the use of transfer factor, topical treatment, and steroid administration. These differences make a final evaluation of the use of retinoids in mycosis fungoides difficult at the present stage. Further studies are needed. (Author abstract) (6 Refs)

33. TRANSFER FACTOR THERAPY IN MYCOSIS FUNGOIDES: A DOUBLE-BLIND STUDY.

Thestrup-Pedersen K, Grunnet E, Zachariae H
Dept. Dermatology, Marselisborg Hosp., DK-8000 Aarhus C, Denmark
Acta Derm Venereol (Stockh); 62(1):47-53 1982

Sixteen patients with mycosis fungoides (MF) were given either active transfer factor (TF) or heat-inactivated TF as additional therapy to topical nitrogen mustard or PUVA. The TF was prepared from nonselected healthy blood donors. The clinical evaluation after 2 yr of therapy showed that among eight patients treated with active TF, none went into complete remission of their disease, four patients had partial remission, one was unchanged, two progressed, and one died of active MF. In the placebo-treated group, five patients achieved complete remission and two partial remission. One patient died early in the trial due to cardiac disease. Immunological studies during the 1st yr of therapy revealed cutaneous anergy towards tuberculin in most of the patients. This anergy did not change during TF therapy and differed from normal lymphocyte reactivity in vitro after tuberculin stimulation. At the start of treatment the patients had diminished levels of T lymphocytes in peripheral blood. A temporary increase was observed in the total number of T lymphocytes in patients after 1 mo of treatment with active TF. After 1 yr the T lymphopenia had disappeared in both groups. The mitogen reactivity of lymphocytes was found to be normal (PHA, PWM) or somewhat reduced (Con A). It is concluded that under the conditions employed in this trial, TF was not able to prevent progression of early mycosis fungoides, when viewed over a period of 2 yr. (Author abstract) (36 Refs)

MALIGNANT LYMPHOMA: CASE REPORTS

34. LYMPHOMA WITH AUTOIMMUNE NEUTROPENIA AND HEPATIC SINUSOIDAL INFILTRATION: A SYNDROME.

Kruskall MS, Weitzman SA, Stossel TP, Harris N, Robinson SH
Dept. Hematology/Oncology, Beth Israel Hosp., Boston, MA, 02215
Ann Intern Med; 97(2):202-205 1982

A relation between lymphoma and autoimmune neutropenia, unlike autoimmune hemolytic anemia and idiopathic thrombocytopenia purpura, has not previously been well documented. We report a patient with a disorder presenting as autoimmune agranulocytosis, splenomegaly, and infiltration of the hepatic sinusoids by lymphocytes. Antineutrophil antibodies were present. Over a 2 1/2-yr period, the illness progressed to an aggressive, poorly differentiated lymphocytic lymphoma with terminal liver failure and fibrosis. Peripheral blood lymphocyte markers identified the tumor as a proliferation of T-cells of the helper class. A review of previous literature disclosed other reports of similar patients who had neutropenia, a lymphoproliferative illness, and hepatic disease. Our case is representative of a previously unrecognized syndrome characterized by autoimmune neutropenia in the setting of a lymphoproliferative disorder of T cells, with a predilection for liver involvement. (Author abstract) (21 Refs)

35. DIFFUSE FOLLICULAR LYMPHOID HYPERPLASIA OF THE SMALL INTESTINE WITHOUT PRIMARY IMMUNOGLOBULIN DEFICIENCY.

Rambaud JC, De Saint-Louvent P, Marti R, Galian A, Mason DY, Wassef M, Light H, Valleur P, Bernier JJ
Inserm U 54, Hopital Saint-Lazare, 107 bis, rue du Faubourg Saint-Denis, 75475 Paris Cedex 10, France
Am J Med; 73(1):125-132 1982

Three cases of follicular lymphoid hyperplasia extending to the whole length of the small intestine are reported in three young adult patients of low economic status. The disease was revealed by chronic diarrhea with malabsorption and/or protein-losing enteropathy. In one patient, all transitional patterns were found between the hyperplastic follicles and a small intestinal multicentric centrocytic-centroblastic lymphoma. No abnormalities in humoral or cellular immunity were found in the three patients. In particular, serum immunoglobulins (except IgG in one case) and plasma cell populations of small intestinal lamina propria were normal. Diffuse follicular lymphoid hyperplasia of the small intestine in the absence of primary immunoglobulin deficiency appears to be a rare condition associated with (or leading to) intestinal malignant lymphoma in most cases. Patients usually belong to the same populations as those suffering from alpha-chain disease. (Author abstract) (34 Refs)

36. DIFFUSE T-CELL LYMPHOMA PRECEDED BY NODULAR LYMPHOMA.

Jennette JC, Reddick RL, Saunders AW, Wilkman AS

Dept. Pathology, Sch. Medicine, Univ. North Carolina, Chapel Hill, NC, 27514

Am J Clin Pathol; 78(2):242-248 1982

A patient with a nodular lymphoma morphologically indistinguishable from follicular B-cell lymphoma subsequently developed a diffuse T-cell lymphoma. This T-cell lymphoma displayed characteristics analogous to mature T-lymphocytes, and typed as a suppressor/cytotoxic T-cell with monoclonal antibodies. The light and electron microscopic morphology of the T-cell lymphoma was similar to that reported for node-based T-cell lymphomas. There was a polymorphous proliferation of variably transformed lymphocytes including immunoblasts. This case could represent either a nodular form of T-cell lymphoma converting to a diffuse T-cell lymphoma, or a follicular B-cell lymphoma preceding, and possibly inducing, a suppressor T-cell lymphoma. (Author abstract) (29 Refs)

37. TWO CASES OF LYMPHOMA OF THE PAROTID GLAND FOLLOWING ABLATIVE RADIOIODINE THERAPY FOR THYROID CARCINOMA.

Wiseman JC, Hales IB, Joasoo A

Royal North Shore Hosp., St. Leonards, NSW, 2065, Australia

Clin Endocrinol (Oxf); 17(1):85-89 1982

Two adult patients are described whom 131I therapy for thyroid carcinoma was followed by the development of non-Hodgkin's lymphoma in salivary glands. Histologically one was lymphocytic and the other histiocytic. The total doses of 131I given were 27 GBq (675 mCi) and 14 GBq (350 mCi), lymphoma presenting 10 and 3 yr respectively after the initial therapeutic dose of 131I. We suggest that the relationship is a causal one, because of the rarity of salivary gland lymphoma and the high dose of radiation to the salivary glands with this mode of therapy. (Author abstract) (14 Refs)

38. THYROID LYMPHOMA WITH ADJACENT NERVE PARALYSIS.

Billie JD, Wetzel WJ, Suen JY

Ear and Nose-Throat Clinic, PA, 1200 Medical Towers Building, Little Rock, AR, 72205

Arch Otolaryngol; 108(8):517-519 1982

Although local nerve invasion in thyroid lesions is most commonly found with anaplastic carcinoma, it does not rule out lymphoma. Open biopsy is most helpful in the diagnosis of lymphomas. Ultrastructural studies are often necessary for confirmation of the diagnosis. Differentiation between lymphoma and anaplastic carcinoma of the thyroid is very important since the treatment is substantially different and the prognosis is much better with lymphoma. To our knowledge, the case presented represents the first case of Horner's syndrome secondary to lymphoma that has been documented in the literature. (Author abstract) (13 Refs)

MALIGNANT LYMPHOMA: SELECTED REPORTS ON ETIOLOGY AND EPIDEMIOLOGY

39. EPSTEIN-BARR VIRUS ACTIVATION WITH EUPHORBIACEAE PLANT EXTRACTS: A POSSIBLE CAUSE FOR BURKITT'S LYMPHOMA AND NASOPHARYNGEAL CARCINOMA.

Ito Y, Yanase S, Morigaki T, Kishishita M

Dept. Microbiology, Faculty Medicine, Kyoto Univ., Kyoto 606, Japan

Excerpta Med Int Congr Ser; 571:423-427 1982

Speculation is raised as to whether Epstein-Barr virus-activating substances generated by Fusobacterium and other anaerobes in the mouth, and diterpene esters in Euphorbiaceae extracts with similar activity, might interact in the mouth to initiate the first step of carcinogenesis, which eventually may lead to Burkitt's lymphoma. Similar chronic inflammation in the nasal cavity and nasopharynx could serve to cause nasopharyngeal carcinoma. (2 Refs)

40. PERSISTENT ACTIVE INFECTION OF EPSTEIN-BARR VIRUS (EBV) IN CARRIER FEMALES OF THE X-LINKED LYMPHOPROLIFERATIVE SYNDROME (XLP).

Sakamoto K, Seeley JK, Purtilo DT

Second Dept. Surgery, Kumamoto Univ. Medical Sch., Kumamoto 860, Japan

Excerpta Med Int Congr Ser; 571:375-379 1982

Among conditions that may follow infection with Epstein-Barr virus (EBV), is malignant lymphoma in males affected by the X-linked lymphoproliferative syndrome (XLP). To test the hypothesis that the variable expression of XLP is manifested in obligate carrier females, blood from 12 obligate carrier females was studied for anti-viral capsid antigen (VCA), anti-early antigen (anti-EA) and anti-Epstein-Barr nuclear-associated antigen (EBNA). All carriers were seropositive to EBV. The reciprocal geometric mean titer for IgG anti-VCA was elevated to 570 in the carrier females compared to 100 in 24 controls. The range of anti-VCA was from 80 to 5,120. IgA class anti-VCA was found in 2/3 of the carriers. All but one of those with anti-VCA of IgA class showed anti-EA, indicative of active infection and immunodeficiency. About one-half of the carriers had persistent anti-EA antibodies. However, the anti-EBNA levels of carrier females were similar to those of the healthy controls. There was no apparent relationship between IgM level and EBV-specific antibody titers. The paradoxically elevated EBV-specific antibodies which tend to persist in obligate carriers of XLP provides an opportunity to define the immunopathology of XLP and to detect carrier females. (17 Refs)

MALIGNANT LYMPHOMA: SELECTED PRE-CLINICAL STUDIES

41. GENERATION OF LONG-TERM T-LYMPHOID CELL LINES WITH SPECIFIC CYTOTOXIC REACTIVITY FOR A SYNGENEIC MURINE LYMPHOMA.

Eberlein TJ, Rosenstein M, Spiess PJ, Rosenberg SA
NIH, Building 10, Room 10N 116, Bethesda, MD, 20205
JNCI; 69(1):109-116 1982

The long-term in vitro growth in T-cell growth factor (TCGF) of murine cytotoxic T-lymphoid cells directed against syngeneic tumor antigens was investigated. C57BL/6 mice were immunized to syngeneic FBL-3 lymphoma by two ip injections of irradiated FBL-3 lymphoma cells. Splenocytes from these animals were injected into mice with disseminated lethal FLB-3 tumor. The injection of cyclophosphamide (Cy) plus immunized lymphocytes significantly improved survival with cure of 53% of 38 animals. In comparison, treatment with Cy alone resulted in 0 to 31 cured and treatment with Cy plus unimmunized cells resulted in 0 of 40 cured (p less than 0.0005). These in vivo immunized lymphocytes were reexposed to FBL-3 tumor in vitro for 5 days in lectin-free TCGF (LF-TCGF). Although in vivo and in vitro sensitized lymphocytes exhibited no cytotoxicity toward fresh FBL-3 tumor cells in an 18-hour 51Cr release assay, expansion of appropriately sensitized cells in LF-TCGF resulted in significant lysis of fresh FBL-3 tumor cells. This significant lysis was specific and lysed syngeneic FBL-3 but not syngeneic MCA-103 fresh tumor targets. This maximal specific cytotoxicity was maintained for 2.5 months. A screening assay was developed that permitted rapid identification and isolation of low-frequency cytotoxic clones with reactivity specific for FBL-3 tumor. Several of these cloned cells were grown for almost 3 months with maintenance of high degrees of specific lysis (as much as 4,500 lytic U/10(6) cells). These cytotoxic lines and clones will be of value for the study of tumor-host immunologic interactions and perhaps for use in adoptive immunotherapy. (Author abstract) (68 Refs)

42. INTERFERON ENHANCES GUANYLATE CYCLASE ACTIVITY IN HUMAN LYMPHOMA CELLS.

Rochette-Egly C, Tovey MG
Unite INSERM 61, Avenue Moliere, 67200 Strasbourg, France
Biochem Biophys Res Commun; 107(1):150-156 1982

Treatment of the human Burkitt lymphoma derived cell line Daudi with electrophoretically pure human interferon alpha (IFA), which causes a rapid increase in the intracellular concentration of cyclic guanosine monophosphate (cGMP), enhances guanylate cyclase activity. The increase in guanylate cyclase activity in IFA-treated cells resembled that induced by 10 milliM sodium azide in in vitro systems. Neither partially purified nor electrophoretically pure IFA had any effect on guanylate cyclase activity in a cell-free system made from Daudi cells, however. These results strongly suggest that activation of guanylate cyclase in IFA-treated cells is mediated via interaction of interferon with its specific cell surface receptor. The increase in cGMP in IFA-treated cells was calcium-dependent and was abrogated by treatment with the cyclo-oxygenase inhibitors aspirin and indomethacin. (17 Refs)

43. BONE MARROW PROGENITOR CELLS OF AKR MICE GIVE RISE TO THYMIC LYMPHOMA CELLS.

Hays EF
Lab. Biomedical and Environmental Sciences, 900 Veteran Ave., Los Angeles, CA, 90024
Leuk Res; 6(3):429-432 1982

Twelve (AKR x DBA/2)F1 mice were given 400 rad and inoculated iv with bone marrow cells from 1-mo-old AKR donors. Six of the 12 mice developed thymic lymphoma between 158-244 days after cell inoculation and irradiation. Lymphoma occurred in three of nine control animals at 265, 280, and 287 days after irradiation. All of the six lymphomas occurring in mice given AKR bone marrow cells were thymic lymphomas. The microscopic morphology of the tumors as seen by hematoxylin and eosin prepared sections showed replacement of thymus, spleen, and lymph nodes by malignant lymphoblasts and infiltration of liver sinusoids and periportal areas with similar cells. One of the three control lymphomas was non-thymic. A retroperitoneal mass, slightly enlarged spleen, and no hepatomegaly were observed, and all lymph nodes were enlarged and replaced by tumor cells. The two remaining control lymphomas grossly resembled those of the experimental mice, but microscopic examination showed cells with pleomorphic nuclei and few mitoses. The microscopic findings in the control mice were in sharp contrast to the findings of large, round nuclei and abundant mitotic figures seen in the lymphomas from the AKR cell-treated mice. Four of the six experimental lymphomas were tested for growth in AKR mice. The lymphomas produced tumors 14-15 days after ip inoculation of 4 x 10(6) cells to AKR recipients. The findings implicate a bone marrow progenitor as a 'target cell' for the age-related development of thymic lymphomas in AKR mice. (7 Refs)

44. CELL SURFACE ANTIGEN PHENOTYPES AND ENZYME EXPRESSION PATTERNS OF TWO MURINE T-CELL LYMPHOMAS DERIVED FROM EARLY AND/OR MATURE THYMUS CELLS.

Dullens HF, Hilgers J, Van Basten CD, De Weger RA, De Heer E, Den Otter W
Dept. Pathology, State Univ. Utrecht, Pasteurstraat 2, 3511 HX Utrecht, The Netherlands
Leuk Res; 6(3):425-428 1982

Expression of cell surface antigens on SL2 and GRSL13 cells and enzyme cytochemistry of murine SL2 and GRSL13 lymphoma cells were investigated. SL2 lymphoma occurred as a spontaneous tumor in DBA/2 mice, and GRSL13 lymphoma occurred as a spontaneous lymphoma in GRS mice. While T200 antigen expression was high on both lymphomas, Thy1 was low on GRSL13 and high on SL2. Significant difference between the two lymphomas was obtained using antibodies 30-G12 (anti-T200) and 30-H11 (anti-glycolipid) with positivity on GRSL13 and no reaction on SL2; a reverse pattern was seen with antibodies 53-7.3 (anti-Lyt1) and 53-6.7 (anti-Lyt2). Since ThB and the glycolipid detected by antibody 30-H11 were expressed on bone marrow cells and since ThB was not expressed at all on peripheral T cells, the antigens are apparently characteristic for the more primitive cells in the thymic series. Results showed that GRSL13 represents a T cell of a more primitive immature type, while SL2 represents a more mature T cell. Enzymes present and clearly expressed in the lymphomas as well as the majority of thymus cells were acid phosphatase, beta-glucuronidase, non-specific esterase, and alphanaphthyl-acetate-esterase. No clear difference was observed between the two lymphomas and the normal thymus cells. (17 Refs)

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